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"SPRAY X-RAY THERAPY" IN POLYCYTHEMIA VERA AND IN ERYTHROBLASTIC ANEMIA*

BY FRANCIS T. HUNTER, M.D.†

IRRADIATION of the body as a whole with high voltage röntgen rays,—diversely termed "total irradiation", "teleröntgenotherapy", "röntgen baths", or "spray therapy", — was first proposed and used by Teschendorf.[1] Since the publication of his paper in 1927, experience has shown that in cases of generalized carcinomatosis and in instances of widespread radioresistant tumors, therapy of this type is no more efficacious than discontinuous irradiation through limited fields. Nevertheless, in the handling of certain radiosensitive hyperplasias and neoplasms widely distributed throughout the body, this form of röntgenotherapy possesses, in theory at least, an advantage over the older method of treatment, in that the whole mass of morbid tissue is evenly and simultaneously subjected to the action of the rays. Accordingly, a number of observers in recent years have employed it in cases of leukemia and lymphoblastoma; but, it must be confessed, opinion as to its usefulness in these conditions is, so far, not uniform.

POLYCYTHEMIA VERA

On the other hand, the results in the few recorded instances of its use in polycythemia vera seem to have been satisfactory enough to evoke mild enthusiasm. First utilized in this malady by Sgalitzer,[2, 3] "spray therapy", according to him, produced in thirty-four cases[4] remissions of from one and a half to five and a half years' duration. None of his three reports, however, contain protocols of the cases or detailed accounts of the blood examinations. Paltrinieri[5] in 1933 reported satisfactory therapeutic results in two cases, but of these, one patient was followed for only ten months, the other for a scant five days,—observation periods obviously too brief to allow proper evaluation of the method. Likewise, Marchal et al[6] have recorded a patient observed over a period of five and a half months, in whom the red blood corpuscles fell from an initial figure of 8,200,000 per cu. mm. to 6,200,000 per cu. mm. after a total dosage of 205 r units. But, since no other investigators have made contributions to the subject, and no original observations on the effect of "spray therapy" in polycythemia vera have yet appeared in the English language, it was thought that a more or less complete report on two patients suffering from this disease, who were given "spray therapy" and closely followed for three years, might be of interest.

CASE 1. *Polycythemia Vera—Multiple Thromboses.* The patient, H. A., was a white, native, housewife, aged forty-nine, who entered the hospital October 27, 1932, complaining of painful, swollen legs.

Present Illness. In 1910, during her second pregnancy, and again in 1915, while carrying her third child, the patient observed transient, nontender varicosities on the mesial side of each thigh. With this exception her medical history was uneventful until about ten months prior to entry, when a red, tender, subcutaneous lesion, 3 cm. in size, made its appearance on the inner aspect of the left leg just above the knee; this was accompanied by swelling of the leg and by a dull aching femoral pain. Some two or three weeks later,—in February 1932,—she suddenly experienced a severe pain in the right chest, sharp in character and exaggerated by inspiration, which gradually decreased in severity, and which at the end of a week's time had disappeared. She was informed, presumably by her medical attendant, that it was a manifestation of pleurisy. In the early part of March, a new subcutaneous nodule, similar to the first, appeared on the right leg, and it, too, was followed by femoral edema and "pleurisy". From that time until entry to the hospital, several lesions of like nature had been noted on the thighs and abdomen, and for the past month both legs had been persistently enlarged.

The *family history*, except for a story of asthma in the mother and of hay fever in one sister, was noninformative.

The *marital history* and the *past history* added no essential facts.

Physical examination showed a well-developed, obese woman with plethoric facies. There was definite choking (2 diopters) of each optic disc and obliteration of the physiological cupping. The retinal vessels were distended and tortuous and there were many hemorrhages into the retinae,—an appearance consistent with thrombosis of both central retinal veins. On each side of the neck, the jugular vein could be palpated like a cord. No variation from the normal could be detected upon examination of the heart and lungs. The blood pressure was 150/90. A red, slightly tender, indurated, subcutaneous lesion, 12 cm. in diameter, was present on the right lower abdomen,—apparently thrombosis of the subcutaneous veins. The liver and spleen were thought to be enlarged. Each ankle showed slight pitting edema. There was no elevation of temperature.

*From the Medical, Pediatric and X-Ray Treatment Departments of the Massachusetts General Hospital, Boston.

Read before the New England Roentgen Ray Society, Boston, February 21, 1936.

†Hunter, Francis T. — Assistant Physician, Massachusetts General Hospital. For record and address of author see "This Week's Issue," page 1159.

Laboratory findings. Examination of the urine revealed no abnormalities. A blood Hinton test proved negative. The basal metabolic rate was plus 2 per cent. The sedimentation rate was 3 mm. at the end of one hour (normal 20 mm.). Blood examination showed: red blood corpuscles 8,500,000 per cu. mm., hemoglobin (Sahli) 125 per cent, white blood corpuscles 12,000 per cu. mm. Except for a polymorphonuclear percentage of 85, the stained specimen exhibited no variation from the normal. The hematocrit reading gave 60 per cent cells; the oxygen capacity was 24.11 volumes per cent.

"Spray therapy" was begun November 11, and was continued through December 7, 1932. The apparatus was operated so as to deliver to the patient about 20 r per hour (measured in air), at a target skin distance of 215 cm., through 0.5 mm. of copper and 4.0 mm. of celluloid; M.A. 4, K.V.P. 200. A total of 304 r was given in eleven sittings. A second course of treatment (with the same arrangement of the apparatus) was begun on January 24, 1933 and completed on February 28, 1933. In this course of therapy 598 r were administered in twenty-six sittings. Thus a total of 904 r was received by the patient in about ten weeks' time.

Present Illness. For the period between 1920 and 1930 he could recall episodes of headaches accompanied by vomiting of material which at times resembled "coffee-grounds". There was a dim recollection of indigestion, and a more vivid impression that he had passed tarry stools on occasion. About two years prior to entry these symptoms subsided to some extent and were replaced by dyspnea and palpitation on exertion. About the same time his attention was called to a mass in the left upper quadrant of the abdomen. Three or four months before entry, he began to feel weak and experienced in the region of the mass an intermittent aching pain, which occasionally radiated to the epigastrium, and which was usually made worse by lying down. He again observed tarry stools and became convinced that the swelling in the left upper quadrant had grown larger. During the past two months there had been a loss of ten pounds in weight.

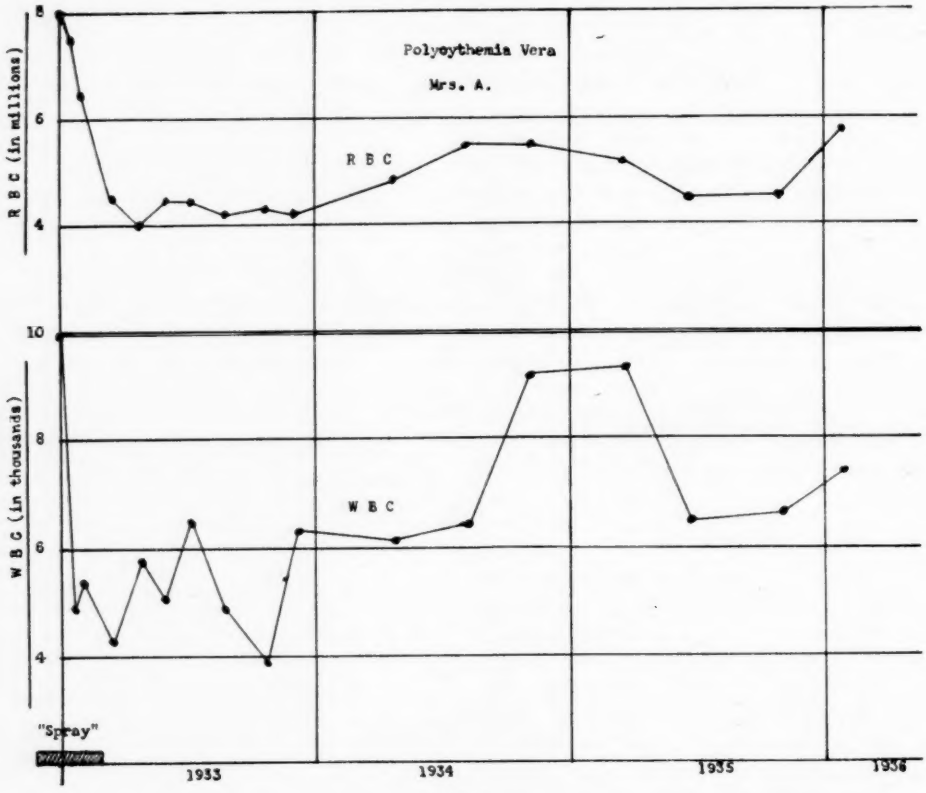

FIG. 1.

Course. This is best seen by reference to figure 1, on which is depicted the erythrocyte and leucocyte counts during the treatment and for the follow-up period of three years. The general improvement of the patient closely paralleled the lowering of the erythrocyte count, and at the last visit she appeared to be normal in every way.

CASE 2. *Polycythemia Vera—Duodenal Ulcer—Pulmonary Tuberculosis (inactive).*

A. G., a fifty-two year old, white, married grocer,—born in this country of Italian parents,—entered the hospital August 3, 1932 complaining of not feeling well and of an aching in the upper left abdomen.

The *family history* and the *marital history* were nonessential.

Past History. Aside from diseases of childhood, he had never undergone a serious illness. For thirty-three years he had experienced, from time to time, migratory arthritic symptoms, consisting of red, nontender swelling about various joints. On three occasions during the past decade, ecchymoses had appeared without adequate cause,—once on the terminal portion of the thumb and twice about the orbit.

Physical examination showed a poorly developed and nourished man with pallor of the mucous membranes. Arteriosclerosis of the peripheral vessels was marked. Examination of the heart and lungs revealed no obvious abnormalities. The blood pressure was 140/80. A slightly tender irregular tumor was visible and palpable in the left side of the abdomen, and this mass, which was thought to be an enlarged spleen, extended to the level of the

umbilicus. The temperature fluctuated between 98° and 100°F.

Laboratory Findings. Urinalysis and the blood Hinton test were negative. Stool examination revealed no traces of occult blood. An intradermal tuberculin test in 1/1000 dilution was negative. Blood examination showed: red blood corpuscles 5,300,000 per cu. mm.; hemoglobin (Sahli) 45 per cent. In the blood smear the polymorphonuclears made up 91 per cent of the leucocytes, and the erythrocytes exhibited marked achromia.

X-ray studies confirmed the presence of a mass, extrinsic to the stomach, in the left upper quadrant of the abdomen. There was a constant deformity of the duodenal cap consistent with ulcer. The lungs showed infiltration and cavitation at the left apex, and plates of the spine revealed marked arthritic changes.

Re-entry to the hospital, March 8, 1933. The patient now complained of heaviness of the head, pounding in the ears, and moderately severe frontal headaches recurring about every ten days. There had been no gastrointestinal symptoms. *Physical examination*, except for a dark red, cyanotic color, gave the signs previously described. *Laboratory findings.* Blood examination showed: red blood corpuscles 10,630,000 per cu. mm.; hemoglobin (Sahli) 125 per cent; polymorphonuclears 85 per cent; red blood corpuscles normal in appearance. The stools showed no occult blood, the basal metabolic rate was plus 41 per cent, and the hematocrit reading gave 65 per cent cells. Re-examination of the chest and gastrointestinal tract by the x-ray revealed no change.

The patient was discharged March 24, 1933 with the diagnosis of polycythemia vera.

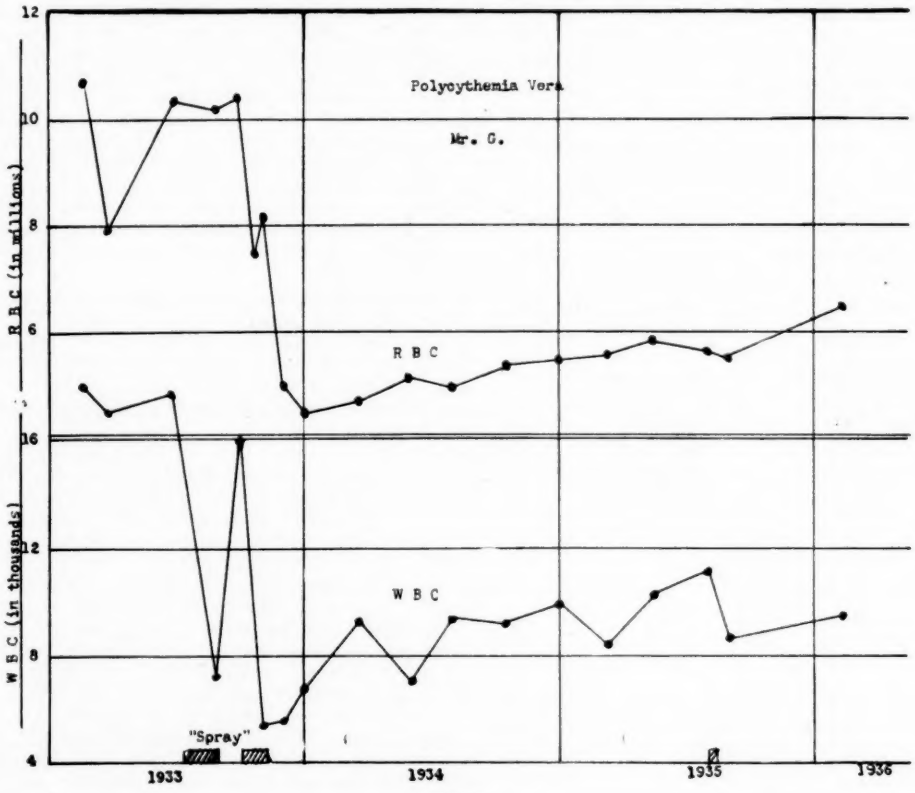

FIG. 2.

The patient was discharged August 21, 1932 with a questionable diagnosis of lymphoblastoma.

Progress. High voltage röntgen therapy to the abdominal mass through a 20 cm. x 20 cm. anterior field, at a target skin distance of 50 cm. was begun in the X-Ray Treatment Clinic on August 23; a total of 600 r was administered in divided doses. Between September 21 and September 26, 800 r additional were given to the posterior abdomen through a field of the same size.

December, 1932. The patient felt much better and had gained seventeen pounds in weight. He now, however, showed injected sclerae, a high color and a suggestion of cyanosis. The red blood corpuscles numbered 6,700,000 per cu. mm.

February, 1933. The patient's color was a deeper red than at the last observation. The red blood corpuscles were 11,375,000 per cu. mm., the hemoglobin (Sahli) 150 per cent. It was thought that the unusual blood picture seen the previous August must have been caused by bleeding from the duodenal ulcer.

"Spray therapy" was given between June 6 and July 20, 1933; but it was subsequently discovered that because of difficulties encountered in computing dosage, the patient had received, during this period, only a fraction of the prescribed amount of therapy. [Note that the erythrocyte count did not fall during this time.] A new course of therapy was begun on September 25 and completed on October 25, 1933, the patient receiving a total of 1192 r in twenty-two sittings. The apparatus was arranged as in Case 1, except that an increase of the milliamperage to 6 raised its output to approximately 54 r per hour. An additional small amount of therapy, totaling 180 r, was administered between July 22 and July 29, 1935 in six sittings.

Course. Reference to figure 2 makes clear the effect of the therapy on the blood picture during the treatment period, and during the three succeeding years. All symptoms disappeared, there was a considerable gain in weight, and the spleen decreased in size. At the present time the patient feels perfectly well.

COMMENT

From the previously reported cases of polycythemia vera treated by "spray therapy", and from the two recorded here, it can be stated that this type of irradiation is definitely superior to the therapeutic agents in common use. Röntgenotherapy through small fields has not demonstrated its practicability as a routine measure. Dangerous drugs, such as phenylhydrazine and arsenic, require constant supervision and cautious administration; even then they often give rise to gastrointestinal disturbances, jaundice, or skin eruptions. Phlebotomy, an unpleasant procedure at best, not only must be performed at frequent intervals, but on occasion is ineffective. And as for daily stomach washes which have been recently suggested, one can only agree with Publius Syrus: "There are some remedies worse than the disease." "Spray therapy", on the other hand, when administered in small doses over long periods of time, has an astonishingly prolonged depressant effect on the blood-forming organs, produces no disturbing clinical symptoms, and may be given without interruption of the patient's daily work. For these reasons, therefore, I believe it to be the treatment of choice in polycythemia vera.

ERYTHROBLASTIC ANEMIA (COOLEY)

Hereditary erythroblastic anemia (Cooley), a pathologic entity manifesting itself in certain infants of Mediterranean parentage, has some histologic points in common with polycythemia vera. Although treated unsuccessfully in the past with röntgen rays through limited fields, prior to the autumn of 1935 it had not been, to my knowledge, subjected to a trial with "spray irradiation". When, therefore, a characteristic case of this curious malady entered the hospital and was sent to the X-Ray Department for an opinion as to the advisability of röntgenotherapy, the hope was entertained that if sufficient depression of the hematopoietic organs could be brought about, the continued escape of immature nucleated red blood corpuscles into the peripheral blood stream might be prevented. It was with this object in view that "spray therapy" was begun.

Through ignorance of the optimal dosage in this condition, the treatment went far beyond the desired result and produced an overwhelming, acute bone marrow depression. The leucocytes fell to 500 per cu. mm. and the platelets almost disappeared from the blood stream. There was an accompanying purpura and an alarming series of epistaxes,—the latter necessitating repeated blood transfusions. When this critical period had passed and the leucocytes and platelets had reappeared in the peripheral blood in more normal numbers, the circulating red blood corpuscles rose gradually but steadily and after some weeks reached a higher level than had been observed at any time prior to irradiation. The amelioration, too, of the child's general condition seemed even more marked than the improvement of the blood picture. Thus the final clinical and hematologic effect of "spray therapy", while perhaps not so striking in this disease as in polycythemia vera, seemed encouraging enough to warrant recording the case.

CASE 3. Erythroblastic Anemia (Cooley).

M. P., seven year old American-born boy, of Italian parentage, entered the hospital September 5, 1935 complaining of pallor and weakness.

Present Illness. The patient had never been well or strong since birth, and had always appeared abnormally pale. At the age of five and a half years, eighteen months prior to entry, the mother became aware that his pallor was increasing and that his strength was failing. Although in the year just past the boy had attended school, he had not felt well enough to participate in games with his playmates and complained that climbing one flight of stairs tired him out. The mother further testified that his interest in food had almost vanished, that his abdomen was gradually enlarging, and that his general condition was becoming progressively worse.

Family History. Two sisters of the patient have erythroblastic anemia and are being observed at the present time in the out-patient department of the Massachusetts General Hospital. Three other sisters appear to be well.

The *past history* revealed no facts of importance.

Physical examination showed a well-developed and nourished boy with sallow complexion, pale mucous membranes, prominent eyes, and Mongoloid facies. He seemed chronically ill. There was slight icterus of the sclera. The chest, although barrel in type, gave no abnormal signs when percussed and auscultated. A loud systolic murmur (? hemic) could be heard over the entire precordium. There was a marked enlargement of the abdomen. The liver edge was palpable 7 cm. below the costal margin, and a visible and palpable spleen with a smooth, firm surface extended to the level of the iliac crest. The body weight was forty pounds.

Laboratory Findings. Nothing abnormal was found in the urine. Blood examination showed: red blood corpuscles 2,540,000 per cu. mm., hemoglobin (Sahli) 28 per cent; polymorphonuclears 56 per cent, lymphocytes 25 per cent, normoblasts 15 per cent, hematoblasts 2 per cent, unclassified cells 2 per cent. The erythrocytes exhibited extreme variation in size and shape, with many tailed forms, microcytes, macrocytes, stippled and polychromatophilic cells; platelets somewhat decreased. The icterus index was 5; the bleeding time five minutes. The blood Hinton test was negative.

X-ray studies showed bony changes in the skull, pelvis and lower extremities characteristic of erythroblastic anemia.

"Spray therapy" was begun on September 10, and completed on September 25, 1935, a total of 360 r being given in fourteen sittings. The apparatus was that used in the treatment of the first two patients, but so arranged that approximately 40 r per hour (measured in air) was received by the patient.

Course. When the crisis (referred to earlier) had passed by, the patient's general condition improved in a manner paralleling the betterment of the blood picture. Figure 3 shows the return of the leuco-

cytes to normal, the augmentation of the red blood count, and the reduction in the absolute number of circulating nucleated red cells. The spleen decreased in size to a considerable extent and subjective symptoms disappeared. At present the child, though still somewhat pale, is bright and active, is gaining weight, attends school without fatigue and plays with gusto like any normal boy of his age.

COMMENT

This single case of erythroblastic anemia treated with "spray therapy" neither invites lengthy discussion nor warrants generalizations. It does demonstrate, however, that irradiation by this method has a rather marked depressant action on the rapidly proliferating erythroblasts in the bone marrow; and that, with the consequent lowered rate of hematopoiesis, fewer immature cells appear in the peripheral blood, an increased number of erythrocytes reach the blood stream, and a definite clinical improvement takes place in the patient. It is, of course, too early to comment on the lasting effects of the treatment, or on the frequency with which it should be repeated. Obviously the dosage used in this case was administered at too rapid a rate. Doses of from 10 to 20 r, given at five day intervals, might possibly produce beneficial results without such a marked effect on the leucoblasts and megakaryocytes. However that may be, the result of "spray therapy" in one case of erythroblastic anemia is presented here with the hope that further observations will be made.

CONCLUSIONS

(1) "Spray x-ray therapy", consisting of 1000 r given over several weeks' time, produced remissions lasting three years in two cases of polycythemia vera.

(2) "Spray x-ray therapy" in small doses in one case of erythroblastic anemia brought about favorable changes in the blood picture and improved the patient clinically.

(3) This form of treatment appears to be the one of choice in polycythemia vera, and deserves further trial in erythroblastic anemia.

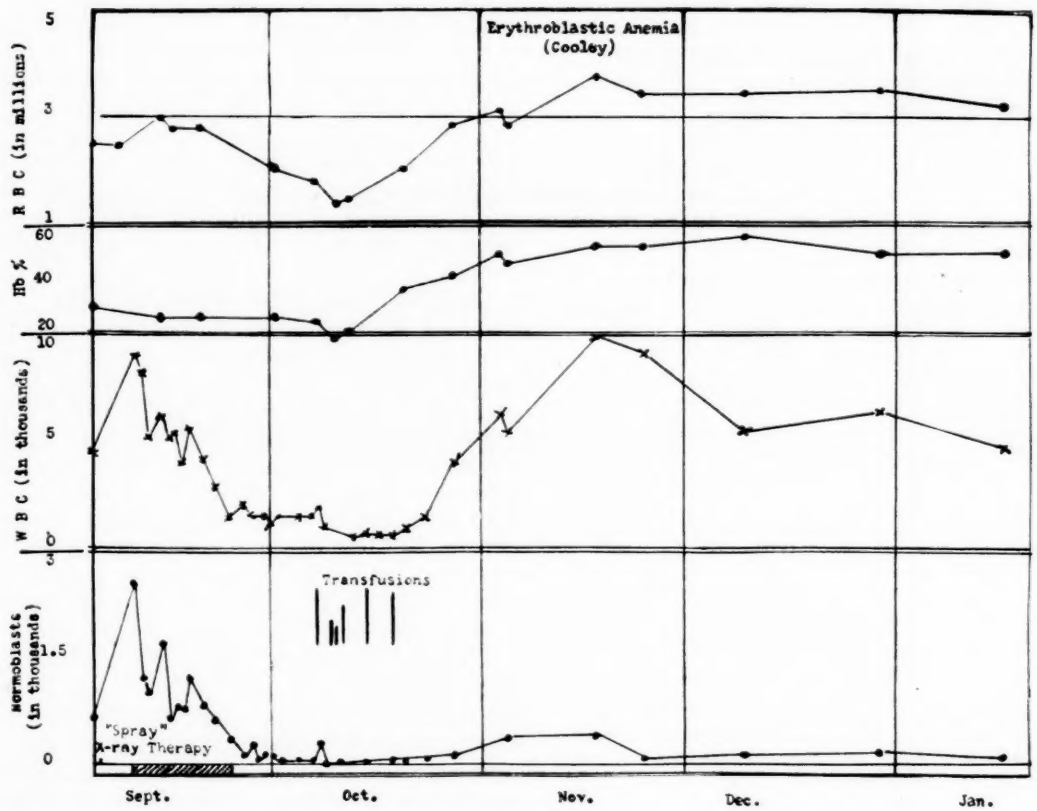

FIG. 3.

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CERTAIN RELATIONS BETWEEN THE PARATHYROIDS, THE HYPOPHYSIS AND THE PANCREAS*

BY BERNARDO A. HOUSSAY, M.D.†

THE present paper will deal only with the manner in which the hypophysis and the pancreas can influence the structure and function of the parathyroids, rather than attempt to consider all of the many relationships which may exist between these glands or their secretory products. It may be noted here that the parathyroids, due to their small size, are frequently overlooked in postmortem examinations; also the microscopical alterations may be passed by, as frequently they are not easy to interpret. These facts explain to a certain extent why the histophysiology of these glands is less well known than that of others.

In 1930 Lascano Gonzalez, in our Institute, found pronounced lesions in the parathyroids of dogs whose pituitary and pancreas had been removed.[37, 38, 42] This finding led us to study the microscopical aspect of the parathyroids and also the blood calcium of (a) hypophysectomized, (b) pancreatectomized and (c) hypophysectomized-pancreatectomized dogs.

THE PARATHYROIDS IN PITUITARY INSUFFICIENCY

Morphology. The development and the maintenance of the normal structure and function of the endocrine glands (thyroids, gonads, adrenal cortex, parathyroids, thymus, etc.) are conditioned by the anterior pituitary, and hypophysectomy results in abnormal changes. In the case of the parathyroids hypophysectomy is followed by regressive lesions which can be seen microscopically, but it is difficult to determine whether the total mass of parathyroid tissue is reduced. Smith[79] found a diminution of the total amount of epithelial bodies in hypophysectomized tadpoles, but apparently there was no marked alteration in their structure. Smith[79] stated that atrophy of the parathyroids occurred in hypophysectomized rats, but in a later paper[80] he did not mention this condition, and Collip[18] was unable to confirm the observation. In the subtotally hypophysectomized hen no modifications have been found;[61] and in the hypophysectomized rabbit there are only slight changes, mainly a decrease in the size of the cells.[85] Livon and Peyron,[53] Aschner,[4] and Collip,[18] saw no changes in the parathyroids of hypophysectomized dogs; on the other hand Koster and Geesink[47] mention having found these glands atrophied, but give no further data on this subject.

We have been unable to find any reports on the structure of the parathyroids in human cases of pituitary insufficiency.

Lesions of the parathyroids have been reported in several papers published from our Institute since 1930. Up to date these glands have been examined in forty-two normal dogs, forty-six hypophysectomized, three hypophysectomized-thyroidectomized and in sixteen with lesions of the *tuber cinereum*.

The parathyroids of the normal, craniotomized controls have a massive, reticular or lobulated structure. The cells are polygonal or globulous and the majority have a clear or only slightly granular protoplasm. In some glands, especially near the surface, groups of dark staining nuclei are found so closely packed together that no protoplasm can be seen around them (Syncitium-ähnliche Zellgrupen). The connective tissue is scarce and in it are seen very fine blood vessels.

The first alterations occurring in the parathyroids of hypophysectomized dogs consist of the following phenomena: the cells decrease in size; the protoplasm becomes dark and granular, and its borders are no longer clearly marked; the nuclei are also reduced in size and the cells are more closely packed, so that they separate from the connective tissue stroma. This gives the structure of the gland a trabecular or cord-like aspect. Later the protoplasm atrophies and finally disappears almost completely, leaving the nuclei in rows or heaps. It is important to note that these modifications are found only in certain parts of the gland, e.g., at one of its poles or sides. In the most advanced degree the protoplasm disappears and only rows of nuclei are left, the meshes of the connective tissue stroma become prominent, and the blood vessels are dilated and sometimes surrounded by a fibrous sheath. In parts of the gland the degeneration of the epithelial cells may be so complete that acellular structureless zones of irregular dimensions and of granular aspect are formed; these stain a rosy violet color.

These alterations are not uniformly distributed, so that in any one animal some of the glands may be almost normal while others may show severe lesions. In the same gland normal and modified regions are to be found side by side. The morphological changes first appear five to fourteen days after hypophysectomy; they then spread and finally become stabilized. The following degrees may be differentiated (figure 1):

(a) *Slight:* uniform cellular atrophy, few groups of closely packed nuclei, trabecular structure. (Figure 2A.)

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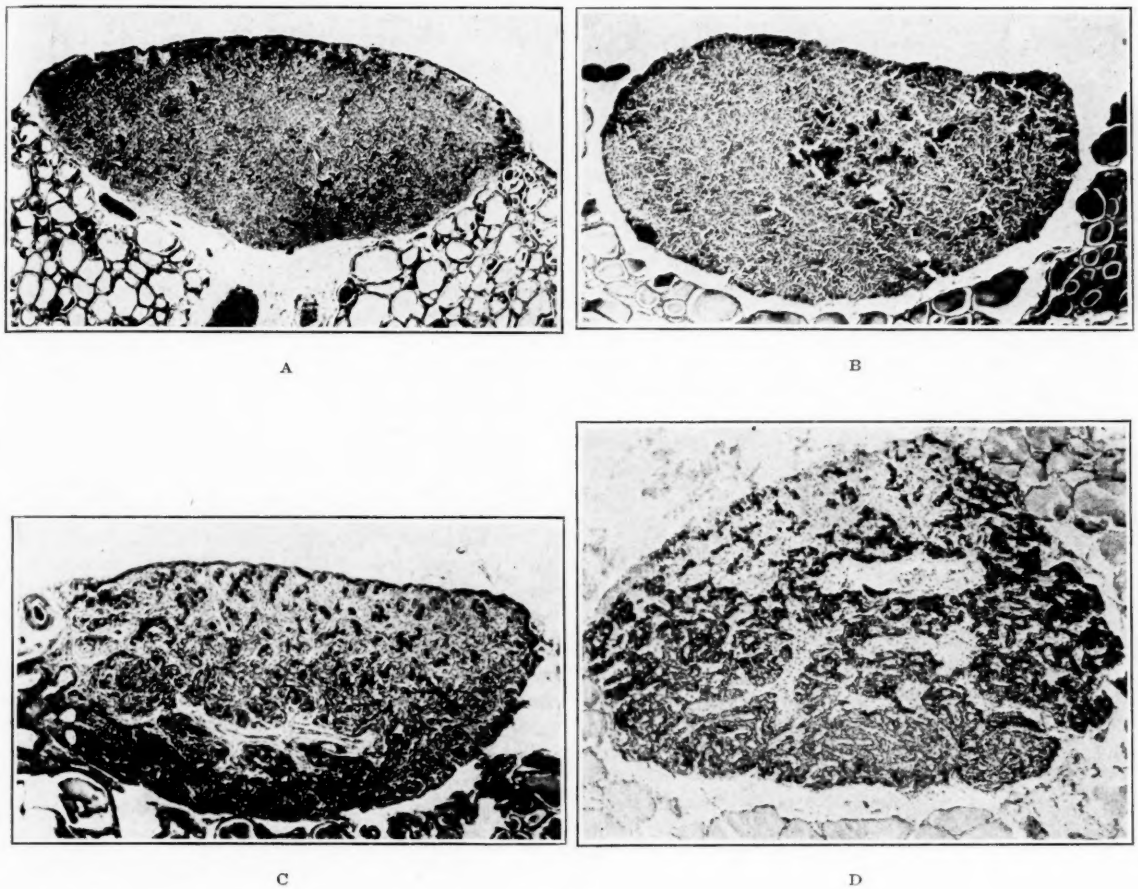


FIG. 1.

Sections through the parathyroid glands of dogs to show the normal structure, A, and the different degrees of alteration following hypophysectomy, namely, slight modification, B; medium, C; and intense, D.

(b) *Medium:* large groups of closely packed nuclei, disappearance of numerous cells, trabeculae of cord-like structure.

(c) *Intense:* numerous groups of closely packed nuclei, disappearance of many cells, cord-like structure, thick connective tissue trabeculae. (Figure 2B.)

(d) *Very intense:* numerous groups of closely packed nuclei, large fields without cells, cord-like structure, abundant connective tissue, numerous and large blood vessels. (Figure 2C.)

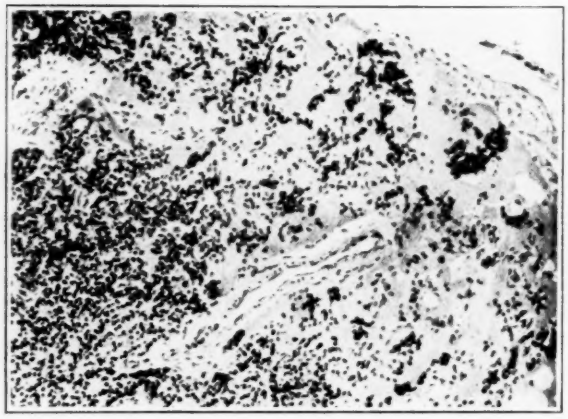
The lesion consists of a simple, progressive atrophy of the cells, with pyknosis and slow disintegration of nuclei. The decrease and retraction of the parenchyma make the connective tissue become more apparent. There is no reduction in the blood supply, on the contrary the blood vessels are large and numerous. There is no granular, fatty or colloidal degeneration. There are no signs of compensatory hyperplasia. The most characteristic features are the global atrophy with darkening of the protoplasm, the accumulation of nuclei (in 66 per cent), the structureless zones, and the great irregularity of the lesions which leave large parts of the gland with little or no alterations. This last fact explains why these animals do not have hypocalcemia. To interpret these lesions it is necessary to examine many cases, make numerous sections of each gland and acquire experience in the study of this tissue. If a careful examination is not made, characteristic lesions, obvious to a skilled observer, may be passed over.

In our series of dogs the following alterations were found:

	No. of Animals	Slight	Medium	Intense	Very Intense	Total	Per Cent
Controls	42	4	—	—	—	4	9.5
Hypophysectomized	46	16	10	4	—	30	65
Hypophysectomized-thyroidectomized	3	—	2	—	1	3	100
With tuberal lesions	16	3	3	—	—	6	37

We have not been able to counteract these effects by the administration of anterior pitui-

A



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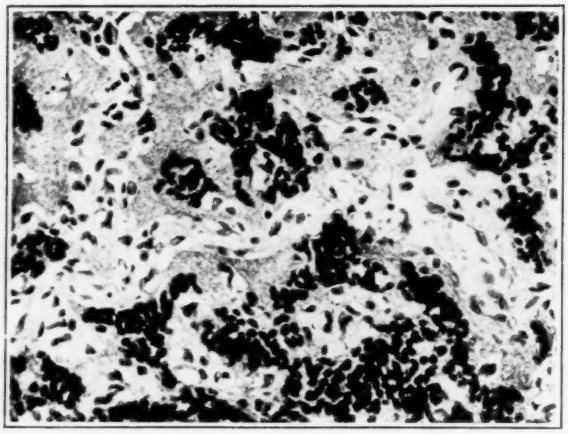


C

FIG. 2.

Sections through the parathyroids of hypophysectomized dogs showing, A, syncytium-like groupings of cells; B, acellular zones; and C, combined syncytium-like grouping and acellular zones.

tary lobe extract, though it has been tried in many cases. It is possible that the doses employed were not sufficient or that the activity of the extract was inadequate.

Calcemia. In spite of the lesions in the parathyroids the plasma calcium was normal in the forty-seven hypophysectomized dogs so far studied in our Institute,[26, 41, 56, 57, 60*] the average being 10.67 Mgm. per 100 cc. in the operated and 10.7 Mgm. per 100 cc. in the controls. In rats also normal values have been found.[17, 84] In two pigeons there was a slight decrease.[71] In rabbits hypophysectomy is followed by a slight increase,[50] but irradiation of the pituitary sufficient to damage the gland does not alter the blood calcium.[10] The toad *Xenopus levis* has a low blood calcium after extirpation of the principal lobe of the pituitary[13, 35, 78] and after gonadectomy.

Parathyroid extract increases the blood calcium of hypophysectomized rats[76] and pigeons[71] to the same degree as it does in normal controls. It also produces a similar proliferation of osteoblasts and new bone formation in hypophysectomized rats as in normal controls.[76] Hypophysectomized rats, however, show a tendency to a negative calcium balance, which is counteracted by growth-promoting pituitary extract.[68] On the other hand, the thyrotropic extract[24, 68] and thyroid administration increase the fecal excretion of calcium with the rise in the total metabolism.

THE PARATHYROIDS IN HYPERPITUITARISM

Parathyrotropic action of anterior pituitary extract. Anselmino, Hoffmann and Herold[3] have shown that anterior pituitary extract produces a considerable enlargement of the parathyroids in rats. There is hyperemia, increase in the number and size of the clear cells, decrease of the dark cells and disappearance of oxyphilic cells.† The same effect is obtained with the alcoholic precipitate of pregnancy urine, which has no thyrotropic activity. Hypertrophy and hyperplasia of the parathyroids have also been obtained in rabbits by the injection of pregnancy urine (Hertz and Kranes, 1934). We have seen this occur in less than half of the dogs injected with anterior pituitary extract (1.4 Gm. per Kgm. per diem of fresh bovine anterior lobe for one week). An increase of the blood calcium lasting several hours has been observed in the dogs injected with this extract, but it does not occur if the thyroids and parathyroids have been removed.[3, 34, 56, 57, 83‡] The

*In two hypophysectomized dogs Koster and Geesink[47] found a lower blood calcium than in their control animals. Since the values in the latter were 13 to 14.2 Mgm. per 100 cc. the observations are hardly significant. Nishida[63] found 10.41 Mgm. in hypophysectomized dogs and 9.97 Mgm. per 100 cc. in the controls.

†Anselmino and Hoffmann have had the kindness to send me their microscopical preparations.

‡This has also been found in the cat[77] and in *Xenopus levis*,[78] but in the rat there is no rise in the blood calcium following this treatment.

parathyrotropic factor has not been completely separated from other hormones but it is known that it is not ultrafiltrable and that it is destroyed by boiling.

The gonadotropic extract aggravates tetany and decreases the blood calcium of thyro-parathyroidectomized bitches, due to the increased secretion of estrin.[59]

Hyperparathyroidism. In seventeen out of 101 published cases of hyperparathyroidism an enlargement of more than one of the parathyroids has been reported. This fact has led to the belief that a stimulating action of the anterior pituitary may be a factor in the etiology of these cases.[1] Of special significance is the finding by Hertz and Albright[30] that the injection of urine from patients with multiple parathyroid hyperplasia is capable of producing parathyroid hyperplasia in rabbits. Urine injection from cases of parathyroid adenoma does not produce this change.

Human hyperpituitarism. In cases of acromegaly some observers have seen enlargement[5, 15, 25, 70] or adenomas[12, 21, 27, 45] of the parathyroids. Cushing and Davidoff[21] noted a marked proliferative activity in one case and parathyroid adenomas in two others. In various postmortem examinations of acromegalics, abnormalities of the parathyroids have been reported. In one curious case of chromophobe adenoma of the pituitary, Lloyd[54] found a simultaneous enlargement of the parathyroids and of the islets of Langerhans. In Cushing's disease cervico-dorsal kyphosis forms part of the syndrome. Osteoporosis and decalcification have been reported in fourteen out of twenty-four cases with postmortem examination in the literature. In nine of the fourteen cases collected by Cushing[20] there were spontaneous fractures, and osteomalacia was present in six.

The condition of the parathyroids is mentioned in fourteen of the twenty-four cases which we have found reported with a postmortem examination: in three cases there was an adenoma,[33, 51, 62, 75] in three the glands were enlarged,[20, 49, 69] in six they were normal,[2, 16, 19, 55, 73] and in one they were atrophied.[82] Lipomatosis associated with other lesions was present in three of these cases and unassociated with other lesions in twenty others.[20, 49, 51, 69, 72, 74, 82]

Cushing[20] believes that the basophile adenoma of the pituitary produces a state of hyperparathyroidism which in its turn causes the bone lesions; Hoff,[33] on the other hand, thinks that in his case the pituitary adenoma was secondary to the hyperparathyroidism. Cushing's opinion meets with various objections: in most of the cases studied up to now lesions due to parathyroid hyperfunction have not been demonstrated; the bony lesions differ from those of hyperparathyroidism; similar bony lesions have been found in cases of primary hyperinterrenalism; the blood calcium and inorganic phosphorus have been found to be normal, or the calcium slightly diminished and the phosphorus slightly increased.[6, 7, 9, 32, 43, 46, 51, 74, 81] The negative calcium balance, observed by Aub in one of Cushing's cases, is common to various bone diseases.[6]

In one of Cushing's cases Aub observed a marked amelioration of all symptoms, including those related to the skeletal system, following irradiation of the hypophyseal region. The negative calcium balance was also diminished.

THE PITUITARY AND PARATHYROID TETANY

Caselli, in 1900, reported that extirpation of the pituitary in dogs suffering from tetany due to parathyroid insufficiency caused a more rapid death without alteration of the symptoms. We removed the thyroids and parathyroids in eight hypophysectomized dogs and found that they developed tetany and died similarly to normal dogs which were thyro-parathyroidectomized.

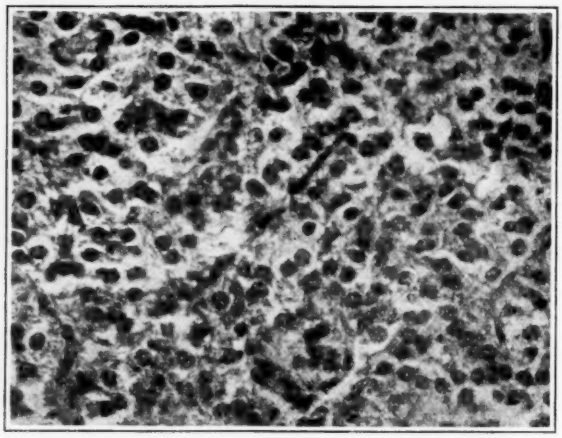
Extract of the whole pituitary gland or of the posterior pituitary can transitorily calm the tetany[11, 36, 40, 64, 65] after an initial exacerbation of the symptoms. The mechanism of this action is not clear, since these extracts do not prevent the reappearance of attacks of tetany or the lethal termination of the condition. We could neither prevent nor cure tetany in thyro-parathyroidectomized dogs, nor prevent the fall in blood calcium, by injecting large doses of an alkaline pituitary extract intraperitoneally for two to three days before or after the onset of tetany.

THE PARATHYROIDS IN PANCREATIC INSUFFICIENCY

Morphology. With R. Sammartino, we have studied the parathyroids of twenty-nine totally pancreatectomized and eight partially pancreatectomized dogs. After one to three days with no insulin the cells of the parathyroids become vacuolated and appear large and clear. (Figure 3.) The vacuoles appear first near the connective tissue trabeculae, following which they increase in size and coalesce. Later the protoplasm liquefies and disintegrates, the nuclei come closer together and form rows contiguous to the trabeculae, and the gland assumes a tubular aspect. In some cells there are also nuclear changes.

When the condition is more intense, the gland decreases in size and presents either an insular or a cord-like structure, due to the decrease in the volume of the cells and the approximation of the nuclei to each other. Some of the latter become pyknotic.

These lesions occur early, are intense, and affect the whole gland. (Figure 4.) The syn-



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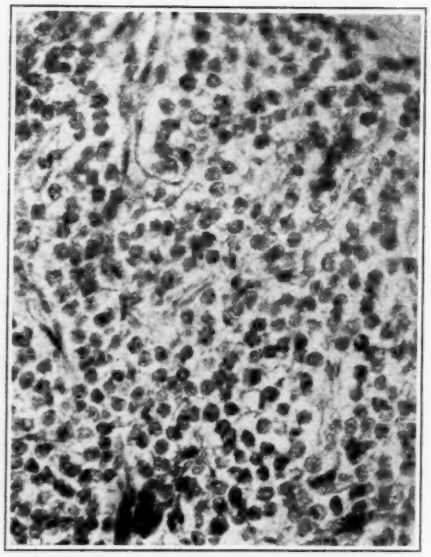

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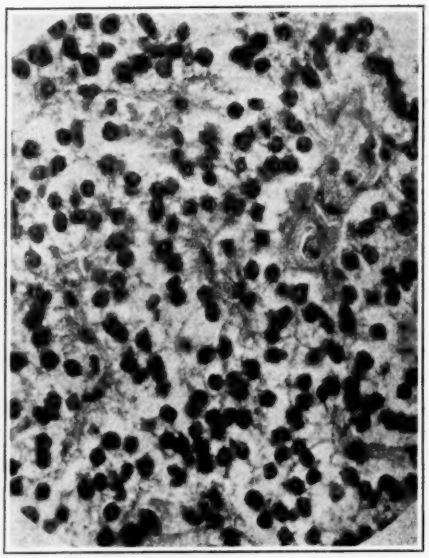

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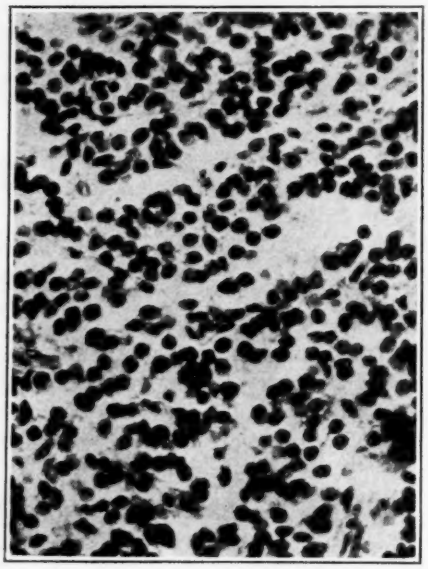

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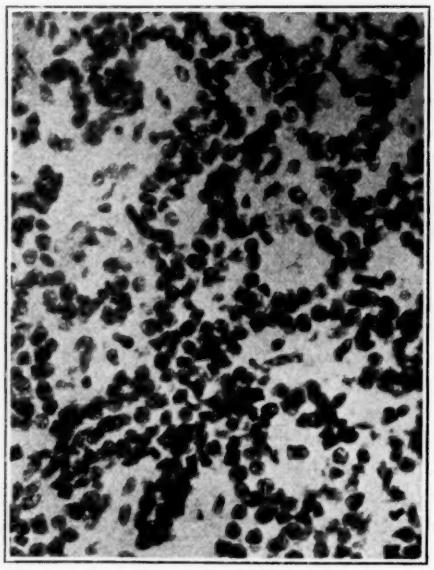

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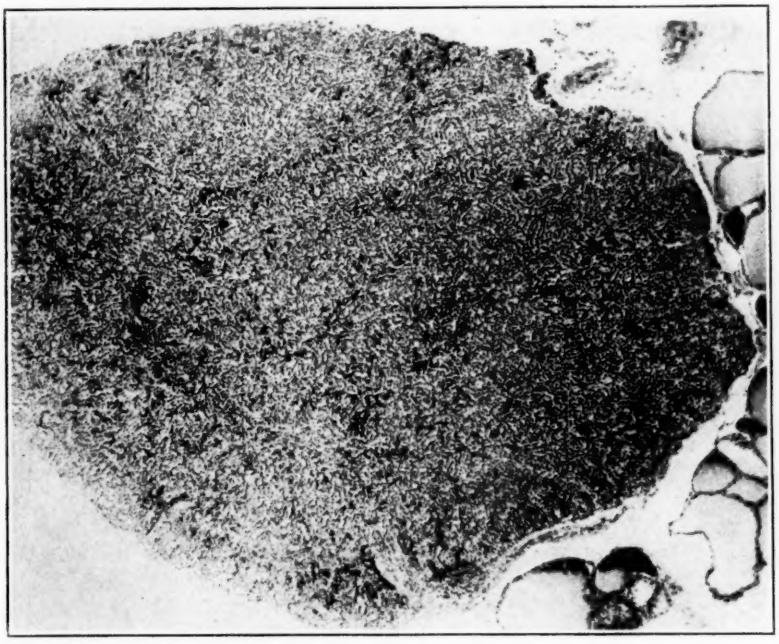
FIG. 3.

Sections through the parathyroid glands of dogs showing A, the normal cytological structure and, B, C, D and E, the progressive stages in the vacuolization and protoplasmic liquefaction which follows pancreatectomy.



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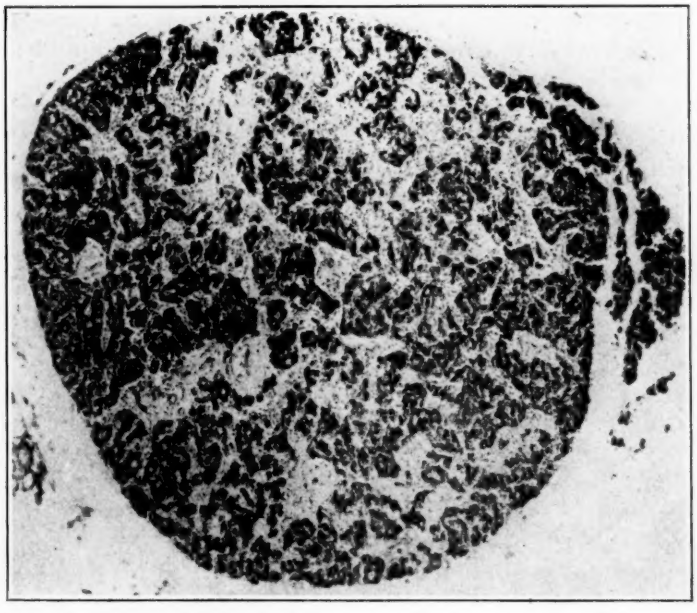

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FIG. 4.

Sections through the parathyroid glands of dogs.
A. Normal.
B. Following pancreatectomy, showing the insular and cord-like structure.

cytium-like accumulations which occur frequently in hypophysectomized animals (66 per cent) are as infrequent in the pancreatectomized (two out of twenty-nine) as in the normals (10 per cent). In contrast with the hypophysectomized animals, where there is a global atrophy of the cells, in the pancreatectomized there is vacuolization and disintegration of the protoplasm.

Calcemia. The determinations made in our Institute on forty pancreatectomized dogs by Marenzi and Gerschman[57, 58] show that blood calcium decreases from the normal level of 10-11.5 Mgm. per 100 cc. of plasma to 8.2-10.5 Mgm. in four days and to 7.3-9.6 Mgm. in seven days. Determinations on twelve dogs showed that in two it fell to 9.2-9.3, in six to 8.1-8.8 and

A

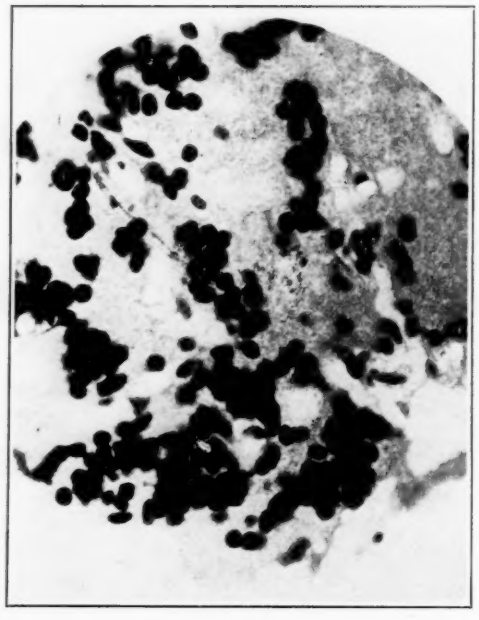

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FIG. 5.

Sections through the parathyroids of hypophysectomized-pancreatectomized dogs.

A. Low magnification, showing the general structure: at *S* there are atrophic zones and syncytium-like groupings of cells; at *C* occur areas of vacuolated and clear cells.

B. Higher magnification, showing the acellular zones and syncytium-like groupings.

C. Magnification as in B, showing clear and vacuolated cells.

in four to 7.3-7.6, the average being 8.2 Mgm. per 100 cc. plasma. The decrease in blood calcium depends on the intensity of the diabetes and is less marked and occurs more slowly or may even be absent if the pancreatectomy is subtotal.

There is also an increase in the inorganic phosphorus which may reach 14 Mgm. per 100 cc. of plasma (the average is 8.8 Mgm.), and a decrease in the sodium and chlorides, the alkaline reserve and the total CO_2 (average 31.9 cc.).

Treatment with insulin prevents the decrease in blood calcium or causes it to rise if already diminished. We did not, however, obtain a return to the original level in our experiments, nor did the histological appearance of the parathyroid glands become normal. This was probably due to the fact that the blood sugar remained elevated and the glycosuria did not completely disappear.

The injection of parathormone caused a rise in the blood calcium (up to 15 Mgm. in one case), just as in normal dogs.

Extract of anterior pituitary lobe was injected into the pancreatectomized animals, but it resulted in an intensification of the diabetes leading to coma and death in one to two days, with a marked hypocalcemia (averaging about 7 Mgm. and in one case falling to 3.9 Mgm. per 100 cc. plasma).

The hypocalcemia and the changes in the parathyroids do not occur in dogs with intact pancreas under conditions of simple fasting, or after the administration of phlorhizin for a week either during fasting or with feeding, even though there is intense glycosuria and loss of weight.

Human diabetes. Kraus[48] has observed parathyroid lesions in some young diabetics, the principal cells being poor in protoplasm, with dark nuclei, giving the appearance of lymphoid tissue. These are the cytological signs of atrophy and functional insufficiency. In adults there is less cellular alteration. According to Jansen[44] the blood calcium is normal in diabetics except in certain isolated cases which have ketonuria. In these it may fall to 8.2—8.5 Mgm. per 100 cc. (as compared with 11.5 Mgm. in normals). He attributes this fall to a loss of calcium in the feces due to the acidosis.

It is premature to attempt to connect the arteritis, cataracts, bony alterations, etc., of diabetics with an alteration in the calcium metabolism and parathyroid dysfunction.

THE PARATHYROIDS IN HYPOPHYSECTOMIZED-PANCREATECTOMIZED ANIMALS

Morphology. We found with Sammartino that the parathyroids in nine hypophysectomized-pancreatectomized animals presented both the lesions found in hypophysectomized and those seen in pancreatectomized animals separately (figure 5). In six such preparations there were abundant syncytium-like groups of cells and structureless, degenerated basophilic zones. At the same time in extensive areas, sometimes occupying the whole gland, there was vacuolization of the cells, the latter becoming big, and vesicular, with transparent protoplasm. This is the appearance of the parathyroid in the early stages after pancreatectomy, and probably the lesions do not develop further as the diabetes is not so intense in the hypophysectomized-pancreatectomized animals.

Calcemia. The calcemia of these animals is lowered as in the pancreatectomized, but the fall occurs more rapidly. Thus, in eight cases after four days, Marenzi and Gerschman[57, 58] found blood calciums of 8.10, 7.6, 8.6, 9.2 and 7.5 Mgm. (average 8 Mgm.) per 100 cc. The inorganic phosphorus rises less (average 5.7 Mgm.) than in the pancreatectomized animals; the alkaline reserve does not change greatly (average 54); the sodium and chlorides decrease, and, because of the hypophysectomy, blood potassium also falls.

GENERAL SUMMARY

In the presence of pituitary insufficiency in the dog there is cellular atrophy in the parathyroids with foci or zones of accumulated nuclei, which simulate cords, and occasionally acellular, basophilic areas. These changes may be the result of general nutritive alterations or of the lack of parathyrotropic hormone.

The blood calcium is not altered, probably because the parathyroid lesion is partial or incomplete.

Anterior pituitary extract increases the size of the parathyroids and their content of clear cells. It also raises the blood calcium; but this rise does not occur when the parathyroids have been removed.

The theory has been put forward that an excess of parathyrotropic hormone may be the cause of human hyperparathyroidism but more observations are necessary for confirmation.

The state of the parathyroids in hyperpituitarism has not been studied carefully in large series of cases. Adenomas have been found in cases of acromegaly, and adenomas or enlargement in some cases with Cushing's syndrome, but in general the parathyroids are normal or lipomatous in these diseases. Whether the origin of the osteoporosis in Cushing's syndrome is due to hyperparathyroidism or to the adrenals or to some other cause is not certain.

Pituitary extracts do not prevent or cure the hypocalcemia and tetany due to parathyroidectomy and the results following thyro-parathyroidectomy are similar in hypophysectomized and in normal dogs.

In pancreatic insufficiency in the dog there is vacuolization, liquefaction and later protoplasmic disintegration of the cells of the parathyroids. The nuclei remain isolated, forming tubes, rows or islets. In three to seven days the blood calcium is lowered to levels between 7 and 9 Mgm. per 100 cc. of plasma and the blood phosphorus increases. Insulin prevents the decrease of the blood calcium, but, in experiments at our Institute, late treatment with insulin, after the fall in calcium had occurred, was not completely effective in raising it to normal, nor was the normal histological appearance of the glands restored. It should be noted, however, that in these experiments overnight hyperglycemia was not controlled and further observations are therefore necessary.

In hypophysectomized-pancreatectomized dogs the lesions due both to hypophysectomy, and to pancreatectomy occur side by side. The lesions due to pancreatectomy are not so severe as in dogs in which the pancreas alone has been removed though the hypocalcemia is similar in the two groups.

The proper functioning of both the pituitary and pancreas is necessary in order to maintain the integrity of the parathyroids. Insufficiency of one or the other of these glands results in different changes. Although proof for the theory is incomplete it may be suggested that in hypophysectomized animals there is a lack of a parathyrotropic hormone, which may or may not be a specific one; whereas, in the pancreatectomized animals, the changes may be due to nutritive disturbances associated with the diabetic condition.

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THE HYPOPHYSIS AND RESISTANCE TO INTOXICATIONS, INFECTIONS AND TUMORS*

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Introduction

In the early days of the study of endocrine glands it was thought that they possessed antitoxic functions. The disorders due to glandular insufficiency were attributed to toxins arising from metabolic processes, or absorbed from the intestine. The toxins were thought to accumulate in the body because of the fact that they were neither destroyed in the gland itself, nor neutralized in the blood or tissues by the glandular secretions. This antitoxic theory has deservedly collapsed, since the supposed toxins have not been isolated, nor has their existence been demonstrated in a way that would explain the functional disorders of the different glandular insufficiencies. On the other hand, several hormones are now known, and some have been isolated in a pure state. These hormones prevent or cure the metabolic and other functional symptoms of the respective glandular deficiencies and, if given in excess, even produce signs of glandular hyperactivity.

The abandonment of the idea of an antitoxic function of the endocrine glands in favor of a hormonal function, has resulted in a loss of interest which reigned about a quarter of a century ago, in the study of the relation between the endocrine glands and immunity. Nevertheless this problem is of importance both in general pathology and immunology.

Very little work has been done on the pituitary from this point of view; probably because there are not many who have access to hypophysectomized animals, and also because it has been only recently that active extracts have been obtained, even though these latter are still very impure and complex.

The pituitary may play a part in immunity and resistance to intoxications in various ways: (1) By direct antitoxic action (intra- or extraglandular). (2) By its action on other endocrine glands. Since the anterior pituitary regulates the thyroids,‡ adrenal cortex,‡ gonads, parathyroids,‡ etc., the activity of these organs is decreased in pituitary insufficiency and increased when this gland is overactive. (3) By action on the hematopoietic or phagocytic organs, e.g., the spleen,‡ thymus,‡ etc. (4) By affecting metabolism and vasomotor reactions, the pituitary influences the resistance of the body to agents which lower the blood sugar and to those which lower the blood pressure. The action of such agents is intense in hypophysectomized animals. For the first of these mechanisms there is no proof, but the second, third and fourth occur in cases to be mentioned later.

Extirpation and destructive diseases of the pituitary produce an experimental or pathological deficiency in those functions which are directly performed by the gland. This deficiency is compensated for or may even be over-compensated for by restitution (implantation of the gland or injection of extracts). Hyperfunction (experimental or pathologic) produces opposite and different symptoms from those of glandular insufficiency. When the action is indirect, through the effect on another gland (e.g., thyroid, adrenal cortex, etc.), disturbances occur which are common to pituitary insufficiency and to insufficiency of the said gland. These disturbances are corrected both by preparations of the affected gland (thyroid, adrenal cortex, etc.) and by extracts of the pituitary which are capable of stimulating the gland (thyrotropic, adrenotropic, etc., pituitary extracts). The last-mentioned extracts are effective only when the respective gland is present and capable of responding to stimulation.

Specific neutralization of toxins or destruction of germs by the pituitary or its secretions has not yet been proved. There are, however, several ways in which it could take a part in immunity. Thus it might increase the general resistance of all the body cells or perhaps of only certain tissues to harmful agents; it might also enhance the capacity for antibody formation, or for the fixation and destruction of germs and toxins. Up to the present it is only possible to say that endocrine glands appear to play a certain rôle in immunity in an indirect way, by means of their metabolic functions or other nonspecific activities, such as stimulation of phagocytosis, or maintenance of the integrity and resistance of the skin, the mucous membranes, etc.

The Pituitary in Infections and Intoxications

Infective Lesions of the Pituitary.

The pituitary may be the site of infectious lesions,[13, 14, 17, 18, 28, 29, 33, 38, 47, 48, 55, 58, 59, 62, 68, 69, 70, 78, etc.] such as septic infarcts and abscesses, which in their ultimate evolution give rise to atrophy or fibrosis, the appearance of the syndromes of pituitary insufficiency and to Simmonds' hypophyseal cachexia.[1, 18, 38, 68, etc.] Circumscribed tuberculous lesions affecting the

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‡Besides the early publications of 1916, 1921 and 1922, etc., numerous studies on these subjects have been performed in our Institute from 1930 to the present date.

pituitary as well as metastatic lesions from distant foci and invasion from neighboring tissues have been described.[1, 5, 10, 20, 26, 36, 42, 44, 48, 50, 51, 52, 54, 63, 64, 68, 69, 74, 77, 84, 88, etc.] Syphilis[1, 8, 9, 10, 15, 21, 22, 24, 30, 32, 37, 45, 46, 48, 49, 51, 60, 62, 65, 67, 68, 69, 73, 75, 80, 81, 82, 83, 85, 87, etc.] may produce gummatous or fibrous lesions in the adult and congenital lesions in children. The Treponema pallidum has been found in the latter. (Duperié, Sabrazés.) Echinococcus[31, 40, 72] and cysticercus[1, 49] infections of the pituitary have also been known to occur. For further details the articles of Kraus[2] and Berblinger[1] should be consulted.

The Pituitary in Human Infections.

The pituitary has been studied macroscopically and, what is more important, microscopically in various general infections in human beings, such as tuberculosis,[19, 26, 48, 56, 65, 77, 79, etc.] typhoid,[25, 28, 41, 77, 79, etc.] diphtheria,[16, 23, 28, 35, 48, 56, 79, etc.] smallpox,[77, etc.] erysipelas,[77, etc.] scarlet fever,[56, etc.] tetanus,[77, 79, etc.] the septicemias,[11, 19, 77, 79, etc.] intestinal obstruction,[77, etc.] pneumonia,[25, 28, 77, 79, etc.] rabies,[57] typhus,[77, 79, etc.] encephalitis lethargica,[41] bronchopneumonia,[25, 28, 77] and also in distemper in dogs.[24] The older observations were made with imperfect staining techniques and it was believed that in acute infections an initial hyperactivity,[25, 79] followed later by exhaustion and hypoactivity (Delille) occurred while in chronic infections there was only hyperactivity. The cytological changes have been described more accurately by more recent workers.

Modifications of the Pituitary in Experimental Infections and Intoxications.

A number of descriptions have been given of the histological changes occurring in the pituitary of animals which had been subjected to various experimental procedures. The procedures used included the following: inoculation with diphtheria bacilli or toxins,[4, 16, 39, 77, 86, etc.] typhoid bacilli,[77] staphylococci,[11] streptococci[11] and tubercle bacilli,[11] also with the toxins of worms[12, 71, etc.] and with eel-serum;[39] ligature of the common bile duct,[39] the intestine[39] and the ureter;[39] injection of pilocarpine;[39, 77, etc.] alcoholic poisoning[66] and production of uremia.[1, 25, 39, 54, 56, 76, 77, etc.] Solely on the basis of interpretations of the histological changes, it has been supposed that there is an initial hyperactivity leading to exhaustion and functional insufficiency.

Functional Changes of the Pituitary During Infections.

The functional changes in the pituitary during infections and intoxications are not accurately known, since no method is available by which the pituitary secretion can be measured in the blood; neither has the relation between the histological aspect of pituitary glands and their activity, as demonstrated by implantation or by injection of extracts made from them, been investigated. Del Castillo, in unpublished work, found that there was no change in the gonadotropic effect of the pituitary of rats inoculated with *Trypanosoma equiperdum* on the immature ovary. The animals were killed eight to twelve days after inoculation with a strain that killed the majority of inoculated rats in ten to twelve days.

Azam[7] and Delille,[25] pupils of Renon, attribute the tachycardia, hypotension, insomnia, anorexia, sweating, etc., of acute infections to pituitary insufficiency, although it is by no means certain that these are the symptoms of such insufficiency. The fact that pituitary extracts produce some rise in blood pressure, strengthen the beat and slow the rate of the heart, increase diuresis, etc., is not enough proof to support their theory.

It has been thought possible that the exaggerated increase in height of young typhoid convalescents might be due to pituitary hypersecretion,[11, 24] though, of course, it might also be due to the direct action of the typhoid bacilli or of their products on the cartilage. Sometimes tuberculous children grow very rapidly when they reach adolescence and show signs of prognathism, but it has not been shown whether these symptoms can be attributed to hyperpituitarism or to a toxic action of the disease on tissue growth.[34, 53] Neither can it be affirmed that the sexual retardation and amenorrhea of tuberculous adolescents are due to overactivity of the pituitary.[53]

RESISTANCE OF HYPOPHYSECTOMIZED ANIMALS TO INFECTIONS AND INTOXICATIONS

Sensitivity to Anesthetics and Hypnotics.

Chloralose anesthesia is not well tolerated by hypophysectomized dogs.[153] In 1932 we started to use ether instead of chloralose and the mortality in the first week after operation dropped from 75 per cent to 15 per cent. On the other hand it is necessary to use a larger dose of chloralose than the usual one to anesthetize hypophysectomized or thyroidectomized dogs which have been previously treated with thyroid (1 to 4 Gm. daily of bovine extract for four to six days). This is also true in the case of hypophysectomized dogs after treatment with anterior pituitary thyrotropic extract. Ether anesthesia, however, gives unsatisfactory results in hypophysectomized toads.

The hyperglycemia due to morphia is less marked in hypophysectomized toads than in the controls, and implantation of the glandular lobe increases it.[139] In the hypophysectomized dog this hyperglycemia is on the average higher

than in the controls, but the difference is not statistically significant.[115] Ten hypophysectomized dogs presented similar symptoms to those seen in twenty controls when given a subcutaneous injection of 30 Mgm. per Kgm. of morphine chloride; one hypophysectomized animal, however, died two hours later in deep coma, while another had convulsions and respiratory failure, but was saved by artificial respiration. These two animals were the only ones which had practically no rise in blood sugar. Diabetogenic anterior pituitary extract increases the hyperglycemia due to morphia in dogs.[139]

Sensitivity to Operations.

Tadpoles deprived of the buccal pituitary anlage have a diminished resistance to unfavorable conditions.[89] Hypophysectomized toads, and those whose glandular lobe alone has been removed, remain active and appear to be in good condition for about three weeks after the operation. Soon after this they become asthenic and this disturbance increases progressively until death occurs.[132] In spite of their apparent good health, from the very beginning they are killed by many operations (e.g., on the testes, thyroids, adrenals and even cloacal ligature), which are well tolerated by the controls.[133, 142, 167, etc.] If, however, these operations are performed five to ten days before the hypophysectomy many animals survive.

Smith[193] stated, and it has been confirmed, that hypophysectomized rats present a general physical impairment, characterized by a lowered resistance to operative procedures, although the wounds heal well.[192] Hypophysectomized rabbits also have a diminished resistance to surgical trauma.[186, 188]

Hypophysectomized dogs are very sensitive to injuries, exposure and bad feeding. They readily become anorexic, which leads rapidly either to cachexia or death in hypoglycemia.[100, 135] Nevertheless with care a large number can be kept alive, even after the removal of one or more other glands besides the pituitary (e.g., ovaries, thyroid and pancreas).

The hypophysectomized - pancreatectomized animals, which have less hyperglycemia, glycosuria, azoturia and acidosis, live longer than the pancreatectomized animals with the pituitary intact, in which the diabetes is more intense. In the former group, with an attenuated diabetes, the wounds suffer less from infection and heal, even though no insulin treatment is given, but they never do so well as the hypophysectomized animals with the pancreas intact.

Sensitiveness to Infections.

According to Aschner[90] hypophysectomized dogs have a diminished resistance to infections, being particularly sensitive to mange, and Cushing[106] also states that hypophysectomized dogs are more susceptible to infections and that their resistance is diminished. We have not confirmed this increased susceptibility having found that mange is readily cured by sulphur,[141] but we have noted that when infected or ill these dogs readily become anorexic, hypoglycemic or cachectic and die. The wounds of hypophysectomized toads (or those without the glandular lobe) are more readily infected and heal slowly and with difficulty (Magdalena, Aubrun, Pasqualini, etc.). Also, their cutaneous glands are frequently invaded by cocci (Aubrun and Porto, unpublished). Hypophysectomized rats show the same sensitivity to caries of the molars as do the normal animals.[191]

Cushing[106] described acute or infectious processes as occurring in seven of his patients, notably in those with a primary hyperpituitarism. There also seemed to be a definite susceptibility to infection in his cases of pituitary basophilism.[210] Atkinson[6] found that out of 1319 published cases of acromegaly only twenty had tuberculosis as well, and that six of these died of the infection.

Sensitivity to Intoxications.

There are four groups of toxic agents which are poorly tolerated by hypophysectomized animals, namely, anesthetics, blood sugar reducing agents, blood pressure reducing agents and those agents which have intense adverse effects on thyroidectomized or adrenalectomized animals.

Blood Pressure Lowering Agents.

The hypersensitivity to histamine and to other shock inducing agents pertains to this group.

Amphibians. Removal of the pituitary does not alter the sensitivity of the frog (*Leptodactylus ocellatus*) to veratrine,[134] or of the toad (*Bufo arenarum* Hensell), twenty days after the operation, to morphine, atropine, curare, and veratrine.[124]

Rats. Three or more weeks after hypophysectomy in the rat the toxic dose of cobra venom is only two-thirds of that necessary to kill the controls.[93] The minimum lethal dose of histamine is halved if the hypophysectomy is total and there is an initial hypotension, but is unchanged if only the posterior lobe has been removed and there is no hypotension.[196] According to Perla[181] the toxic dose of histamine for hypophysectomized rats (one to ten weeks after operation), which show atrophy of the internal part of the adrenal cortex, may be one third, or even only one fifth of that for normal rats. When a sufficiently large part of the anterior lobe is left there is no alteration in the adrenal cortex or in the sensitivity to histamine. Perla believes that the increased sensitivity is due to hypofunction of the adrenal, particularly as

treatment with cortin increases the resistance to histamine, although it does not modify the adrenal atrophy.

Putnam[182] found that a dose of glycine which did not affect the controls caused a decreased metabolism and death in six to twelve hours in hypophysectomized rats.

Dogs. Ferrer Zanchi[118] injected several dogs with a suspension of dead typhoid bacilli. The eight controls survived, but two out of six hypophysectomized animals died, one an hour after receiving 2,500 million bacilli per Kgm., the other twenty-four hours after receiving 500 million per Kgm. This is not surprising since hypophysectomy in the dog produces a slight lowering of blood pressure and a slower recuperation of the normal blood pressure level after bleeding.[101] This slight hypotension has been observed in the rat[196] and is much greater in the toad.[177] Braier[100] noted that injections of B. Coli vaccine caused a less marked rise of the basal nitrogen and creatinin excretion in hypophysectomized dogs, than in the controls, but the rise of temperature was similar in both groups.

Agents Acting Through the Thyroid.

Anterior pituitary extracts, through their thyrotropic action, cause great sensitivity to anoxemia in rats, guinea pigs,[146] and mice.[190] This sensitivity is not observed when the thyroids have been previously extirpated.[146] It may be remarked that hypophysectomized rats tolerate anoxemia more or less as the normal animals do. (Chiodi and Rietti, unpublished.)

The fall in body temperature provoked by novocaine is reduced or prevented in guinea-pigs,[190] and anesthesia by chloralose is somewhat impeded in the dog, by treatment with thyrotropic pituitary extract.

It is known that the resistance of the white rat to the toxic action of acetonitrile is increased by the ingestion of thyroid. (Reid Hunt's effect.) Injections of thyrotropic preparations of the anterior pituitary lobe produce a similar effect,[173, 176, 178, 179, 190*] because they stimulate the thyroid to greater activity. This effect of anterior pituitary extracts has not been observed in thyroidectomized animals.[178, 179] The serum of men[175] and dogs[125] after treatment with anterior pituitary lobe increases the resistance of rats to acetonitrile, but the serum is without effect in the absence of the thyroid. Oehme, Paal and Kleine[176] believe that the active substance is other than the thyrotropic principle of the anterior pituitary, for it appears to be active *per os,* and does not cause histological changes in the thyroids. Posterior pituitary extract also increases the resistance to acetonitrile, without stimulating the thyroids.[154]

Hypoglycemic Agents.

In 1924 Magenta and I found that hypophysectomized dogs are very sensitive to the hypoglycemic action of insulin. Later, with Biasotti and Braier, we found that in these animals a number of different agents readily produce hypoglycemia, with severe symptoms such as convulsions and coma leading to death. This can be prevented by early treatment with glucose, posterior pituitary extract or adrenalin, it being necessary sometimes to repeat the treatment. The hypoglycemia can also be prevented by treatment with anterior pituitary extract for two to three days. It should further be noted that hypoglycemic crises occasionally occur spontaneously in hypophysectomized animals, whether the pancreas is present or not. They are frequent during the secondary fall in blood sugar which follows the hyperglycemia of adrenalin during fasting, and are constant after several days of fasting and also after the injection of phlorhizin or insulin.

Injection of phlorhizin produces fatal hypoglycemia in fasting hypophysectomized dogs[135] and in hypophysectomized toads.[113] This is prevented by feeding the dogs on a protein or carbohydrate diet, but not by fat diets.[97, 184] Treatment with alkaline anterior pituitary extract, before and during a fast of five to six days, prevents the hypoglycemia and death following phlorhizin.[137] Fasting hypophysectomized dogs, after adrenalin hyperglycemia, have an accentuated secondary hypoglycemia, giving rise to hypoglycemic crises.[100, 162]

Aschner[90] believed that although hypophysectomized dogs have a diminished resistance to intoxications, they tolerate subcutaneous injection of adrenalin better than the controls, since they do not develop local necroses and they show a lower glycosuria. Braier[100] injected adrenalin intravenously (0.5 Mgm. per Kilogram in twenty minutes) in fasting hypophysectomized dogs, and found during the first six to seven hours a slightly larger decrease in the excretion of nitrogen and urea than in the controls. There was also a lower hyperglycemia, with a marked secondary hypoglycemia, which gave rise to convulsions in three out of five cases; two of these were saved by treatment, but the other died during the night. When the animals were fed, the hyperglycemia was the same or greater than in the controls. In dogs and men suffering from pituitary insufficiency, Lucke[162] observed a much greater rise in blood sugar following adrenalin, followed later however by a larger fall and a higher renal threshold. In hypophysectomized rabbits the hyperglycemia occurs more slowly and is not so great as in the controls.[120, 156]

*Rietti could not confirm this, but his mice reacted very irregularly to acetonitrile.

The extreme sensitivity of hypophysectomized animals to insulin was discovered by us.[143] Doses, which in the controls cause very slight lowering of the blood sugar with no symptoms, cause an intense hypoglycemia in the hypophysectomized animals, with convulsions and coma invariably ending in death, unless intense and repeated treatment is carried out. This extreme sensitivity to the hypoglycemic and toxic action of insulin has been observed in dogs,[94, 95, 109, 117, 121, 123, 143, 148, 155, 162, 164, etc.] cats,[166] monkeys,[127] rabbits,[104, 105, 120, 157, 186, 187, 188] and man,[91, 108, 126, 162, 165, etc.] but apparently does not occur in birds;[129] it is also observed in hypophysectomized-pancreatectomized dogs (Regan and Barnes;[183] Houssay, unpublished data). It does not occur in dogs with severe lesions of the basal or retro-hypophyseal part of the tuber cinereum,[143] or in rabbits with the midbrain excised.[130]

According to Geiling and his collaborators the sensitivity to insulin is due to deficiency of the posterior pituitary lobe, but on the basis of our experiments we attribute it to anterior pituitary deficiency. Extracts of the posterior lobe can, to a certain extent, counteract the hypoglycemia and its severe symptoms in the dog[123, 143] and toad,[145] though vasopressin may not be efficacious in the rabbit.[105] Animals with inactivated adrenal medulla, which are hypersensitive to insulin, can also be successfully treated with posterior lobe extract.[122]

The protective action of the anterior pituitary lobe extract is very potent, far more so than that of the posterior lobe extract. It is able fully to counteract the sensitivity to insulin and also to raise the resistance both in hypophysectomized and normal toads,[145] dogs [114, 164*] and rabbits.[104] The anterior pituitary extract requires one to two days to increase the resistance,[114] and therefore is not efficacious in animals already in convulsions and coma.[143]

This protective action also occurs in thyroidectomized-hypophysectomized animals (di Benedetto, Houssay, etc.). The sensitivity of thyroidectomized rabbits and dogs to insulin[104] (Houssay, etc.) is greatly increased if hypophysectomy is also performed. For this reason we can exclude the explanation that diminished resistance to insulin following hypophysectomy is due to hypothyroidism.

It has been thought that this diminished resistance might be due to adrenal insufficiency,[96] because adrenalectomized animals are hypersensitive to insulin,[160, 161] and in pituitary insufficiency there is some atrophy of the adrenal cortex. The following objections may be raised against this theory. Anterior pituitary extract has a diabetogenic action in pancreatectomized toads, in adrenalectomized toads and in dogs lacking the adrenal medulla. It also protects these latter from insulin. According to Barnes, Dix and Rogoff, hypophysectomized animals require more adrenalin to prevent convulsions than do those with denervated adrenals. They interpret this observation as showing that hypophysectomized animals do not liberate adrenin during insulin hypoglycemia. On the other hand, Cope and Marks[104] demonstrated that there is adrenin secretion, for which reason they believe that the anterior lobe of the pituitary maintains the glycogenolytic action of adrenin normal.

There are insufficient observations to draw definite conclusions regarding modifications of the sensitivity to insulin in the diabetes of acromegalics. Some authors have observed an increase in the resistance to insulin,[110, 162, 168, 195, etc.] others have found it the same as in other diabetics,[98, 103, 128, 150, 158, 159, 185, 197, etc.] and even hypersensitivity has been described.[169]

Our opinion is that in pituitary insufficiency a hormone is lacking which plays an important rôle in carbohydrate metabolism; hypersensitivity to insulin is due to the absence of this hormone which acts as a stimulating agent for the production of glucose.

Antitoxic Action of the Extracts.

Much work has been done to find out if pituitary extracts can neutralize poisons or increase the resistance of animals to these agents, but the results are not conclusive. Delille[112] tried injecting pituitary extract and various poisons (potassium arsenate, atropine, mercury cyanide, strychnine, human urine) together and separately, but obtained no definite results. Marañon and Aznar[170] state that posterior pituitary lobe extract prevents the toxic action of strychnine in the guinea pig, so that convulsions and death do not occur. These results have not been confirmed by our experiments.[140] Mariante[172] stated that posterior lobe extract masked the toxicity of morphia, but this also was not confirmed by our experiments in guinea pigs and pigeons.[131, 149]

Phagocytosis and Opsonins.

There are a number of scattered observations on the relation of the pituitary to phagocytosis and opsonins of which the following may be mentioned. Carbon dioxide does not produce leucocytosis in hypophysectomized guinea pigs, but if these animals are treated with pituitary extract, they respond normally.[102] The injection of extract of horse pituitary causes a transitory increase in the phagocytic power of the leucocytes and later a diminution.[171] Injection of hypophysin increases the complement in the serum.[161] Pituitrin lowers the opsonic index

*The commercial extract used by Lucke, of unknown preparation, has posterior pituitary lobe properties, i.e., it has an immediate slight glycemic action which does not occur in the absence of the adrenals.

against staphylococci and tubercle bacilli in rabbits.[194]

Parodi (unpublished work) in our Institute has found a marked decrease in the phagocytic powers of the polymorphonuclear leucocytes in the blood of hypophysectomized dogs; using Radsma's modified method he found that 50± 1.9 per cent of the leucocytes ingested starch in the controls, but only 20 ± 5.2 per cent in the hypophysectomized animals. Peritoneal injection of alkaline extract of anterior lobe greatly increases phagocytosis, but this cannot be considered a specific action, as extracts of muscle and kidney will also do this. It is possible that the diminished phagocytosis found in hypophysectomized animals is due to hypothyroidism.

Antibody Formation.

Borchardt[99] states that injection of pituitrin raises the agglutinating power of the serum in animals or men injected with typhoid bacilli. Cutler,[107] however, found an equal formation of these agglutinins in normal and in incompletely hypophysectomized guinea pigs, and also an equal formation of hemagglutinins and hemolysis on injection of chicken erythrocytes. He further showed that neither ingestion nor intraperitoneal injection of pituitary extract altered the course of immunization.

Ferrer Zanchi[118] in our Institute immunized four hypophysectomized dogs and five controls with doses of 2,000 to 5,000 millions of dead typhoid bacilli per Kgm. of body weight. The agglutination curves and maximum titres were similar in both groups.

Savino,[189] also in our Institute, immunized five normal and seven hypophysectomized dogs with diphtheria anatoxin during twelve weeks. The individual titres of the sera tested every two weeks, showed a more rapid immunization in the hypophysectomized animals, the serum of which always reached a higher final antitoxic value. The average was 38 ± 6.1 A. U. for the hypophysectomized, compared with 26 ± 5.5 A. U. for the controls, a difference of 12.3 ± 2.6 A. U. This may be explained as due to hypothyroidism,[119] to hypersensitivity, to slower absorption of the anatoxin, or to general nutritive changes.

In contradistinction to Jungeblut and Engle,[151] Hudson, Lennette and King[147] found that gonadotropic pituitary extract did not cause the appearance of any activity antagonistic to poliomyelitis virus in the serum of monkeys, nor did it increase the resistance of these animals to intracerebral inoculation.

THE PITUITARY AND CANCER

Tumors of the Pituitary.—The pituitary frequently is the site of adenomatous proliferation or of true adenomas of acidophilic, basophilic, chromophobic or mixed types, which give rise to more or less specific symptoms. Malignant adenomas or adenocarcinomas may also occur. Besides these, angiomas, fibromas, teratomas, adamantinomas, etc., have been found. There is a special group of tumors known as tumors of the pituitary canal, which consist of craniopharyngiomas and teratomas.[1, 209, 210, 211, 220, 238, 275, etc.] In addition, metastases from various origins occur in the pituitary[230, 236, 238, 266, 274, 280, etc.] giving rise to certain symptoms (polyuria, etc.). When sarcoma is implanted into the gland in the rabbit it does not proliferate as much as in other tissues.[227]

The Pituitary in Cancerous Patients.

Various histological[1, 201, 215, 233, 236, 261, 265, 273, 279, 280, etc.] changes have been described in the pituitary gland found at autopsy on cancerous patients, e.g., increase in the principal cells,[233] increase[215] or decrease of the basophiles,[238] increase in the weight of the gland and in the number of the eosinophiles,[280] signs of hyperactivity of the anterior lobe, and of hypoactivity of the posterior.[273]

In rats with subcutaneous implantation of tumors, there is an increase and vacuolization of the basophile cells of the pituitary, with enlargement of their Golgi apparatus. The changes are similar to those produced by castration, although the sexual cycle is not affected. If these pituitary glands are then implanted into immature rats it can be demonstrated that they have an increased gonadotropic activity.[225] If the cancerous implantation is made into the uterus there is a larger increase of the eosinophile cells of the pituitary and less of the basophiles, and the pituitary appears like that of pregnancy or after the injection of estrin.[225]

Hypophysectomy and Cancer.

Hypophysectomy before or after implantation of tumors causes a retardation of their growth in rats[199, 262] but does not completely stop it,[243, 255, 269] although it has been observed occasionally that shrinkage occurs and fewer of the implants take.[244, 262, 263] There are also fewer metastases, but the resistance of the animals is diminished.[244] In hypophysectomized rabbits also a diminished growth of implanted sarcoma has been observed,[227] although with partial hypophysectomy tar carcinoma may develop more rapidly than in the controls.[234] Irradiation of the pituitary with x-rays diminishes the growth of cancer in rats,[203, 247] but it has not been proved that this treatment produces any real change in the gland.

Gonadotropic Substances in the Urine of Cancer Patients.

The urine of certain cancer patients will cause ripening of the follicles in the ovary of immature rats and mice.[198, 281, etc.] Zondek attributes

this effect to a substance he calls prolan A. This occurs in 60 to 80 per cent of cancers of the female genital apparatus[198, 208, 212, 216, 221, 222, 281, etc.] and almost constantly in cases of moles or chorioepitheliomas.[198, 204, 205, 218, 221, 228, 229, 235, 248, 252, 253, 260, 267, 281, etc.] In the latter there may be as many as 200,000 to 700,000 rat units per litre, which is of great diagnostic value.[205, 229, 241, etc.] In cases of testicular tumors, particularly in those of embryonic nature, enormous quantities of gonadotropic substances occur,[209, 214, 215, 218, 226, 228, 277, 281, etc.] which are described as prolan A, but differ from this. The high content found in moles and tumors compared with the small amount in the pituitary, leads one to the conclusion that it originates in the tumors and not in the pituitary; this is also borne out by the differences in the action of prolan A and anterior pituitary extracts.

Carcinogenic Action of Pituitary Extracts.

Hofbauer[231] insists repeatedly on the danger of anterior pituitary extracts, since prolonged administration in guinea pigs produces hyperplasia of the endometrium and precancerous lesions of the uterine neck. Overholser and Allen[251] also found atypical epithelial proliferation, and possible metaplasia, which seemed to be precancerous lesions; other investigators[206, etc.] do not admit that these are precancerous.

Action of Pituitary Extracts on Cancer.

Posterior pituitary extracts (pituitrin, etc.) have no influence on the growth of implanted tumors or human cancers.[203, 219, 237, 257, 271, 273] With several anterior lobe extracts various results have been obtained, depending on the injected substances, the type of tumor, and the rapidity of its growth; in some cases an accelerating effect was observed;[203, 219, 223, 227, 255, 258, 272, etc.] in others there was no alteration. The inhibitory action on tumor growth by prolan A described by both Zondek and Hartoch[282] has received some confirmation,[207, 212, 242, 250, 264, etc.] but other investigators have not observed this effect, or else obtained merely a nonspecific weakening in growth.[223, 224, 232, 239, 240, 278, etc.] The disturbing effect on tumor growth *in vitro* described by Reiss and Hochwald,[256] Kriesch and Victorisz[240] has not been confirmed.[249]

GENERAL DISCUSSION

The existence of a direct antitoxic or antiinfectious action of the pituitary gland or its secretions has not been proved, but the gland can modify the resistance of the animal by its metabolic action, its regulating action on the thyroid or adrenal and on the vascular or nervous systems.

The gland can show certain histological changes during infections or intoxications, but their functional significances are not understood. It has been thought that the increased growth in typhoid convalescents or sexual retardation and amenorrhea in adolescent tuberculous patients, may be due to functional changes in the gland but as yet there is no proof of this.

Anesthetics and hypnotics are not tolerated well by hypophysectomized animals, and after operation some species are more susceptible to infections, poisons of the nervous system (cobra venom, morphia, chloralose), blood pressure lowering agents (histamine, etc.) and blood sugar lowering agents (insulin, phlorhizin, etc.). Hypophysectomy, because it produces hypothyroidism, provokes a decrease in phagocytosis and accelerated formation of antitoxins (in dogs), the agglutinin production not being changed. The thyrotropic hormone of the anterior pituitary, by stimulating thyroid activity, causes hypersensitiveness to anoxemia in rodents; in the mouse an increased resistance to acetonitrile and in the dog a slightly increased resistance to chloralose occur.

The pituitary can be the site of benign or malignant new growths, also of metastases. The structure of the pituitary is modified in patients suffering from cancer. Hypophysectomy retards, but does not prevent the growth of tumors and diminishes the number of implantations which take; probably this is due to a metabolic action which should be studied. The urine of cancerous patients (especially cases of uterine tumors, moles, testicular tumors) has a powerful gonadotropic activity. Pituitary extracts can accelerate the growth of certain tumors. In some cases prolan A has an inhibitory action but its specificity and its practical importance are doubtful.

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FOODS CONTAINING ARSENIC AND LEAD

The Department of Agriculture has consistently maintained that foods containing added arsenic and lead in amounts held by qualified scientific opinion to be poisonous or deleterious constitute a definite menace to public health and, under the pure food law, are subject to action. As the result of intensive activities over a period of many years the Food and Drug Administration encounters today relatively few interstate consignments of fruits or fruit by-products containing dangerous quantities of lead and arsenic.

The Washington Dehydrated Food Company was found guilty in 1933 in the Federal court in Yakima, Washington, of a violation of the Federal Food and Drugs Act in shipping in interstate commerce stocks of apple chops carrying residues of poisonous lead and arsenical sprays which might render them injurious to health. The firm later marketed apple chops containing lead and arsenic in amounts deemed by eminent toxicologists to be capable of injury to health. One of these shipments involved a consignment destined for export to France. The Government instituted seizure proceedings when lead and arsenic in such amounts were found, taking the position that the pure food law does not sanction the practice of making foreign countries a dumping ground for foods not measuring up to the criteria of fitness set for our own country. The lower Federal court in that instance, however, ruled against the Government, holding that the shipment fell within a proviso in the food law exempting, under certain conditions, violative shipments consigned to foreign shores. The court also expressed doubt as to the deleteriousness of the material.

An outgrowth of this adverse decision was the institution of a suit for damages by the president of the Washington Dehydrated Food Company against administrative officials of the Department of Agriculture who, in carrying out their duty, had reported the facts as to the arsenic and lead content of the export shipment. The civil suit for damages resulted in a hung jury and is of vital interest to every consumer since in its larger aspects it involved the question as to whether a Federal officer, in the discharge of his official duties under the Food and Drugs Act, can be held personally liable for damages for reporting facts to his superiors in the event of an adverse court decision under the Food and Drugs Act. The action in St. Louis is the most recent chapter in the various legal actions which have grown out of shipments by the Washington Dehydrated Food Company.—*Bulletin*, U. S. Department of Agriculture.

COOK PORK WELL TO PREVENT TRICHINOSIS

Reports received by the Department of Agriculture of several recent cases of illness and some deaths from trichinosis justify a repetition of the warning to cook pork thoroughly before serving. The parasites occur in a small percentage of hogs, which themselves suffer no apparent inconvenience. But the meat of such hogs, unless well cooked, constitutes a considerable danger to human health.

The assumption that pork which has passed inspection by a federal organization is safe even when eaten raw or undercooked is erroneous. There is no test that will show definitely whether trichinae are present in a sample of pork, except in some cases of severe infestation. Certain products that are customarily eaten without cooking in the home are given a special processing at federally inspected establishments, and are free from live trichinae. Pork products of the kind that ordinarily are cooked in the home are not processed in meat-packing establishments, since thorough cooking is a complete safeguard.

When infested pork is eaten by human beings in a raw or insufficiently cooked state, the trichinae are set free in the digestive tract where they give rise to numerous young worms. The latter invade the muscles, thus causing the painful disease, trichinosis, which somewhat resembles typhoid fever, meningitis, and several other diseases that are characterized by fever. Severe cases of this disease are likely to result in death. — *Bulletin*, U. S. Department of Agriculture.

MENORRHAGIA OCCURRING AT THE ONSET OF CATAMENIA IN A PATIENT WITH THROMBOPENIC PURPURA

Report of a Case

BY ARTHUR STERN, M.D.*

SINCE Werlhof in 1781 first described essential Thrombopenic Purpura, many syndromes, characterized by a diminution in the number of platelets, have been described and several classifications proposed. That most commonly accepted[1] consists of two main divisions:

1. Symptomatic Thrombopenic Purpura and
2. "Essential" Thrombopenic Purpura, the latter so termed because no specific etiological factor can be found to explain the lack of platelets in the blood stream. Very briefly, the characteristic findings in this second group (Werlhof's disease) are those of spontaneous hemorrhage into the skin and mucous membranes, a fall in the total count of platelets, prolonged bleeding time, normal clotting time, nonretractile clot and increased permeability of capillary walls.[2]

Many theories have been advanced to explain the thrombopenia and hemorrhagic tendencies. As usual, their multiplicity bespeaks their inadequacy. Denys[3] in 1887 first noted the thrombopenia and suggested it as the main factor in the causation of the hemorrhages, but other investigators[4] have reported several cases in which the other cardinal symptoms were present, including hemorrhage, but in which the platelet counts were normal or only slightly reduced. They were of the opinion that increased permeability of capillary vessels is the essential feature. Others have proposed theories of "splenic toxicity" with inhibition of megakaryocytes in the bone marrow, qualitative changes in the platelets and increased phagocytosis of platelets by the cells of the reticulo-endothelial system.[5, 6, 7]

One of the phenomena noted in essential thrombopenia is excessive menstruation, usually in the form of menorrhagia, often associated with severe and sometimes fatal consequences. A cursory review of the literature discloses many cases of this type reported in the foreign literature but relatively few in this country. Menstrual abnormalities are usually investigated from an endocrinological or gynecological viewpoint. It is probably true that few clinicians think of blood dyscrasias as an etiologic factor in their production. The rapid, almost fulminating course and the effective although nonspecific treatment available for these patients, make it important that they be recognized fairly early.

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REPORT OF CASE

First admission: December 1, 1930.

N. M., a white Italian child was eight years old when first admitted to the Worcester City Hospital. She was a full term, normally delivered baby with an uneventful infancy except for whooping cough at one month of age. Her tonsils and adenoids were removed at four years of age without bleeding. There was no history of purpura, hemophilia or any other familial disease. About one year before entry, many small "black and blue" marks had appeared on both legs. Since then she had never been free from at least one ecchymotic area on her body. About one month before entry she ran into a playmate. Ecchymosis of her face and severe nosebleed followed this episode. After that she suffered from recurrent epistaxis. There was also bleeding from her gums when brushing her teeth. Physical examination showed a well-developed and nourished child. There were ecchymotic areas over her right shoulder and both lower extremities. The liver and spleen were not palpable. Laboratory data: R.B.C. 4,070,000, W.B.C. 11,800, Hgb. (Dare) 60 per cent. A smear showed great paucity of platelets and a count gave 16,000. Bleeding time was twelve minutes and clotting time eleven minutes. The clot retracted in three hours (venipuncture). Serum calcium was 9.1 mg. and phosphorus 4.4 mg. Calcium lactate and iron ammonium citrate were given as symptomatic treatment and the patient was discharged on the twelfth day. Platelet count on discharge was 46,000.

Second Admission: May 18, 1932.

She had been well until the day of entry when she developed severe epistaxis "staining fifteen diapers". Because of the uncontrollable hemorrhage she was brought to the hospital. Examination at this time showed moderate pallor. There were ecchymotic areas ranging from pin-point size to that of a silver dollar on the arms, legs and chest. R.B.C. 3,940,000, W.B.C. 16,400, Hgb. 60 per cent (Tallqvist). Platelets 68,200. She was transfused twice followed by cessation of the epistaxis. Attempts to find a bleeding point on the nasal mucous membranes were unsuccessful. Discharged on the nineteenth day.

Third Admission: December 5, 1932.

She had had a tooth extracted the previous day and there was subsequent hemorrhage of alarming proportions for which hospitalization was sought. Physical examination was unproductive of positive findings except for slight pallor and an oozing tooth socket which stopped bleeding promptly upon application of a pack. Bleeding time six minutes, clotting time four and a half minutes. No other laboratory work done. Discharged in three days.

Fourth Admission: August 6, 1935.

The patient had been symptom free until three weeks before admission when she came down with a "cold". Two weeks before entry she had begun to bleed from the gums and this had continued up to the time of admission. Examination at this time showed only the signs of an upper respiratory infection and also several hemorrhagic spots on the buccal mucous membrane. There was also oozing at the gingival margins. R.B.C. 4,560,000, W.B.C. 6,600, Hgb. 75 per cent (Tallqvist). Platelets 70,000.

Bleeding time ten minutes, clotting time three and a half minutes. The patient was treated symptomatically for her upper respiratory condition and was discharged on the third day.

Fifth Admission: November 26, 1935. She is now thirteen years of age.

Since discharge five months previously, she had not been well, complaining of continual weakness. Her catamenia began eight days before entry, for the first time, and continued until her admission into the hospital, with the passage of large clots daily. For the past month she had had daily attacks of epistaxis each morning upon arising. Examination disclosed a blanched, sallow appearance of her face and mucous membranes. There were several ecchymotic areas below the knees bilaterally. The blood pressure was 110/60. She was observed closely for nine days, during which time she had several attacks of profuse hemorrhage from the vagina with the passage of large blood clots, followed by intervals of only slight bleeding. On the ninth day she received 300 cc. of citrated blood and subsequently was transfused three times. In the meantime she was put on supportive treatment of calcium gluconate, one dram t.i.d., ferrous sulphate, grains 3 t.i.d., cod liver oil, drams one t.i.d.; also a high vitamin and high caloric diet. On the twelfth day she was given radiation over the spleen (200r) and received the same dose every second day for two more treatments. Her blood picture was followed closely (chart 1). On the eighteenth day her vaginal bleeding ceased and on the twenty-fourth day a splenectomy was performed under ether anesthesia. Convalescence was uneventful and there was no further bleeding. She was discharged on the forty-fourth day, under the care of her family physician.

CHART 1

LABORATORY DATA ON FIFTH ADMISSION

Date	R. B. C.	W. B. C.	Hgb.	Platelets	Bleeding Time	Clotting Time	Reticulocytes
11-26	4,250,000	8,400	70 (T)*	114,000	2 min.	5 min.	.15%
12-7	2,900,000	6,600	50 (S)†	67,250	4½ min.	4 min.	
" 11	1,970,000			31,520			
" 15	3,310,000	5,950	55 (S)	66,200			
" 18	3,370,000		45 (S)	67,400			.20%
" 23	2,750,000	8,050	50 (S)	108,000			
" 27	3,350,000		65 (S)	134,000			
" 30	3,610,000		65 (S)	240,000			
1-1	3,930,000	19,850	65 (S)	255,000			
1-3	3,520,000	8,200	65 (S)	250,000			.17%
1-7	3,840,000		65 (S)	350,000			
2-27	3,800,000		65 (S)	76,000	½ min.	½ min.	

*T=Tallqvist.
†S=Sahli.

COMMENT

Essential thrombopenic purpura is rarely a surgical emergency. Only in the presence of intractable hemorrhage as from the nose or uterus does the problem of treatment become acute. While there is wide disagreement at present on the proper treatment of this disease, most authorities agree that in the early mild forms, supportive measures, including calcium in some form, concentrated vitamins, rest and large doses of iron, deserve an adequate trial. In the acute fulminating cases where the patient is in danger of exsanguination, the problem is different: something must be done quickly. During the past years the operation of splenectomy has attained prominence with a preponderance of favorable reports. Some mention of irradiation over the spleen has been made recently but no conclusions as to its effectiveness have been made. In the present case, bleeding ceased after the second exposure to x-rays, but there had been two transfusions previously so that results are inconclusive. Payne[8] maintains that splenectomy should be done as early as possible to forestall the appearance of aplastic changes in the bone marrow and offers an index of operability in the white blood count and number of reticulocytes; if these are normal or elevated, he states, the chances of cure from splenectomy are good; if depressed, splenectomy is contraindicated. Transfusions, of course, are indicated preoperatively, as often as necessary until the patient's optimum condition is reached and are sometimes effective in lessening or even stopping the menorrhagia.

SUMMARY AND CONCLUSIONS

1. A case of menorrhagia with the first menstrual period is reported in a girl thirteen years of age, who had been known to have essential thrombopenic purpura for the past five years.
2. Treatment consisted of a preoperative course of calcium, iron and vitamins with frequent transfusions and a mild course of irradiation over the spleen, followed by splenectomy.
3. Splenectomy is the treatment of choice in chronic cases, providing the Payne index of operability is satisfactory.
4. Irradiation of the spleen deserves further investigation as a palliative or curative measure.

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CASE RECORDS
of the
MASSACHUSETTS GENERAL HOSPITAL

ANTE MORTEM AND POST MORTEM RECORDS AS USED IN WEEKLY CLINICAL-PATHOLOGIC EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 22231

PRESENTATION OF CASE

A sixty-seven year old unmarried white woman was admitted complaining of blurring of vision and drowsiness.

The patient was perfectly well until about six months before entry, at which time she began to have blurring of vision and drowsy spells. The latter would manifest themselves by causing her to drop off into brief naps at odd intervals, occasionally while conversing with another person. At about the same time she began to stagger occasionally while walking. She had one severe headache lasting for about half a day at the onset of her illness but there were none thereafter. After about two months she began to take "potash" as medication but this caused her mouth to dry up and she discontinued it after a month. She was unable to taste anything for several months afterward, however. At the onset of her illness the patient had gradual swelling of her entire face and neck, and the left side of her face seemed to burn at times. This apparently gradually subsided, for it was not discernible at the time of her admission. About three weeks before coming to the hospital she withdrew considerable money from the bank, took a taxi from an outlying town into Boston, and made several unusual purchases, spending in all about $800. Her actions were surprising and unaccountable to her family but no further details were noted. Her mental state was placid and she evidently noted no abnormality.

Physical examination showed a well-developed and nourished female in no discomfort. The pupils were equal but irregular. They reacted sluggishly to light. The right fundus was obscured by medial opacity, but the left was normal. Peripheral vessels were thickened and tortuous. The lungs were normal except for a slight diminution in intensity of breath sounds in the right axilla. The heart was negative. The blood pressure was 130/70. The abdomen was distended and tympanitic. There was slight tenderness in the right upper quadrant but the findings were otherwise normal. Reflexes were symmetrically equal.

The temperature was 99°, the pulse 95. The respirations were 30.

Examination of the urine was negative. The blood showed a red cell count of 3,850,000, with a hemoglobin of 75 per cent. The white cell count was 12,200, 84 per cent polymorphonuclears. Reticulocytes numbered 3.5 per cent and the red blood cells had a volume slightly greater than normal. The nonprotein nitrogen of the blood was 28 milligrams. A Hinton test was negative. A lumbar puncture done with some difficulty showed blood-tinged fluid. The initial pressure was 150 and the dynamics were normal. A count showed 1,452 cells, of which 1,442 were red blood cells, 2 monocytes and 8 lymphocytes. The ammonium sulphate ring test was positive and the total protein was 47 milligrams. The spinal fluid sugar was 76 milligrams and the Wassermann test was negative. A basal metabolic rate was +17 per cent. An electrocardiogram showed a low T_1 and slight inversion of T_2, T_3, and T_4. The serum protein was 4.5 grams. Examinations of the stools were negative.

Following her entry the patient became perfectly rational and offered no complaint at all. Her temperature fluctuated between 99° and 100° and the pulse rose to 100. Examination on the third day showed dullness over the right lower lung area and a friction rub and râles were audible.

An x-ray examination of the chest showed hazy, rather homogeneous dullness at both bases which obliterated the costophrenic angles and faded out rapidly above. There was a triangular area of dullness at the posterior aspect of the right side of the chest which had the general size and shape of a collapsed lower lobe. The heart and mediastinum were displaced toward the right with inspiration and slightly toward the left with expiration. The heart shadow was partially obscured but appeared slightly enlarged in all diameters. The aorta was tortuous and there were no mediastinal masses. A skull plate was negative.

A needle was inserted into the right lower chest and a small amount of bloody fluid was removed. Culture of this material showed gram-positive filamentous branching organisms. Histologic examination showed only acute inflammatory exudate. About this time she developed edema of both the upper and lower extremities which increased progressively. There was no respiratory difficulty, the patient was perfectly calm, and her appetite was unimpaired. At the end of the second week she developed a mouth condition which was termed thrush. During the succeeding week she developed a gradually progressive dyspnea, the white cell count rose to 27,000 and the temperature to 102°. She died on the twenty-third hospital day.

Notes on the History

Dr. Frederick T. Lord: This patient evidently had no mental symptoms following her entry to the hospital. She had some elevation of temperature, 99° to 100°, and a pulse to 100.

Putting these physical signs together, she has diminished breathing, dullness and friction rub, but nothing is said about bronchial breathing, egophony or whisper.

X-ray of the chest was done. We might see the films at this point.

X-ray Interpretation

Dr. George W. Holmes: The skull was examined and I think was essentially negative for a person of her age. She has some thickening here but that is not important. We would interpret these films as normal. The pineal gland is in the usual position.

We have a series of films of the chest. As described in the note, the right lung field was distinctly smaller than the left. The diaphragm was high and partially obscured by fluid. The costophrenic angle is not visible but it looks as if there might be a small amount of fluid there. In this area there is a shadow of increased density which might represent a partially collapsed lobe. The heart shadow is enlarged. The aorta is normal. The lateral view does not give much added information. These were small films with an attempt to show the detail of the structure around the lung. I cannot get any information from them.

I think we would have to say that the x-ray of the skull was negative, that the chest showed a small amount of fluid in both bases, elevation of the right diaphragm with incomplete expansion of the right lung, and a mass near the root of the lung which might be partially collapsed lung. I think we have pretty good evidence of bronchial obstruction. The air is not getting into that lung.

Further Notes on the History

Dr. Lord: The history is meager in the omission of a statement regarding such respiratory symptoms as cough, dyspnea, pain and wheezing. In view of the anemia, it is desirable to know if there was numbness of the extremities and a smooth tongue.

As the patient was rational without complaints after admission and the neurologic examination without significant findings, I am inclined to regard the cerebral symptoms as of functional rather than of organic origin, but it would be desirable to know the field of vision, sensation and ataxia, including Romberg.

Regarding the laboratory findings, primary anemia is suggested by the large red cells and approximately normal color index, and makes it desirable to know if the red cells were oval, the platelets diminished and the results of a gastric analysis. The high reticulocyte count may be due to regeneration of blood spontaneously or after the administration of liver. The ratio of white to red cells in the systemic blood is about one to three hundred and, in consequence, in the spinal fluid about five white cells are to be expected from admixture with blood. As there were only about ten in all in the spinal fluid, the cell count is probably without significance. The positive globulin test, the slightly elevated total protein and the sugar may be disregarded under the circumstances and, on the whole, the spinal fluid may be regarded as negative.

The electrocardiogram is abnormal with low T_1 and inverted T_2 and T_4. Inversion of T_3 is not significant, but the low T_1 and inverted T_2 and T_4 may be said to be of somewhat ill omen. The elevated basal metabolic rate probably has no special import under the circumstances.

We come to the most significant of the laboratory findings, i.e., the presence in the bloody fluid obtained from the chest of nothing histologically but an acute inflammatory exudate and by culture and smear a gram-positive, branching, filamentous organism. For the identification of this organism, such further data are necessary as a description of the culture, information regarding growth with or without access of air and at room or incubator temperature and whether the gram-positive organisms are acid- or alcohol-fast.

Differential Diagnosis

With the data at hand, I am inclined to say that the patient has arteriosclerosis, a lenticular cataract and an anemia with some features suggesting pernicious anemia. The physical and x-ray findings suggest a plugged right lower lobe bronchus. This naturally raises the question of malignant disease among other causes of bronchostenosis, and a complicating inflammatory process in the lung supplied by the occluded bronchus. The neurologic disturbance early in the course of the disease raises the question of possible metastatic cerebral malignancy or metastatic cerebral inflammation.

With respect to the nature of the inflammatory process in the chest, we must consider the possibility of an infection with the group of organisms which show branching filaments in culture. In this connection I am handicapped by the limitation of available data to the morphology and staining reaction of the organism in culture.

There is a group of organisms which are found in tissue and exudate as round or oval cells. One of these, the cryptococcus, can at once be excluded because of multiplication in culture by budding without the formation of

mycelium. Sporotrichosis is usually confined to the skin and subcutaneous tissues. The sporothrix is rarely demonstrable in the tissues or exudate as oval bodies, but is usually first found in cultures which show a gram-staining, branching mycelium and spores. The absence of any mention of spores here and the pulmonary site of the disturbance are against sporotrichosis. The growth in cultures of the blastomyces and coccidioides immitis is yeast-like with the formation of branching, mycelial elements. As no conidia or segmentation is mentioned, these organisms can with probability also be excluded.

The type of organism here falls, with probability, into one of two groups, the actinomyces or the streptothrix. I may say with respect to these organisms that there is an unfortunate confusion in terminology. The term actinomyces bovis (Harz) should, in my opinion, be restricted to anaerobic organisms of the Wolff-Israel type. These organisms, the cause of both human and bovine infection, in tissues form compact colonies composed of branching, gram-staining, filamentous organisms with radially disposed, club-bearing filaments and grow in cultures under essentially anaerobic conditions at incubator and not at room temperature.

There is another and quite different group of organisms found in fresh material as isolated, branching, gram-staining filaments, or a loose aggregation of interlacing filaments, without true club formation, but at times club-shaped swelling of the terminal portion of the filaments and growth in culture under aerobic conditions at room or incubator temperature. The terminology for this group is confusing. In accordance with the principles of nomenclature "nocardia" is tenable, but common usage appears to make the term "streptothrix" acceptable.

There is a tendency to include all branching, filamentous organisms forming colonies with radiating filaments and clubbed terminal portions under the term actinomyces and to use such designations as "actinomyces", "streptothrix" and certain others as synonyms. This is unfortunate as the two organisms are widely separated in biologic peculiarities and give rise to diseases which are quite different in their mode of origin and in their clinical picture.

It is obvious, with the data at hand, that a distinction between these two organisms cannot be made and I may say that the infection falls into the group of either actinomycosis or streptothricosis.

There is one other matter which merits some attention, and that is the development under observation of a disturbance in the mouth termed thrush. Thrush is not an uncommon complication of severe illnesses and I am not inclined to relate the mouth and lung disturbance in any way.

Clinical Discussion

Dr. Henry R. Viets: I know the answer to the problem so I will not say more than just a word about the onset of this rather remarkable illness. This patient was one of four maiden sisters living very quietly in a town fifty miles away and none of them had ever had any signs of mental disease. Their family physician was a well-known practitioner who had known the family for a long time and, although there is a little indication that something happened to this patient before this episode three weeks preceding entry to the hospital, except for the swelling of the face, it seems probable that the other symptoms were not well substantiated. This patient suddenly one morning went to the local bank, drew out some money, went fifty miles to Boston in a taxi, made unusual purchases, such as a barrel of sugar, bought two fur coats for her sisters, and came back at eleven o'clock at night, having spent well over eight hundred dollars. For a quiet, retiring, maiden lady who had never done anything but attend church affairs and things around the town, this was an extraordinary procedure and made us think we were dealing with an acute psychosis. I saw her on that account a few days later. When she was seen neurologic examination was entirely negative, and general examination was also negative as far as I could make out. She had had no respiratory symptoms previously and nothing to call attention to a lung disease. She was mildly confused, did not know her doctors and was not quite sure what hospital she was in. She had various plans about taking her sisters on extensive trips and so forth, and she said she had the money and wanted to do something for the family. There was a vague state of euphoria that went along with the confusion. Then she was transferred here to the Baker Memorial and the rest of the story you have heard. While she was here she was still more or less confused and was not quite sure where she was. She still had ideas about buying expensive presents, taking trips and so forth. She was co-operative and remained in bed. A few days later signs in the chest were discovered and a tap done.

Dr. Frank T. Hunter: I think I can answer a few of Dr. Lord's questions. As to the one about the physical examination of the lungs, I saw her on the second day and my findings were definitely those of fluid at the right base, possibly some at the left, with diminished voice and breath sounds and dullness to flatness.

In regard to the blood picture, the cell volume was only slightly elevated by the hematocrit method and it brought up the question whether she had pernicious anemia on top of something else. The reticulocytes were 3.5 be-

fore liver was given. She was given liver with the idea that if she did have pernicious anemia we had better lose no time in starting treatment. No gastric analyses were made.

As to the chest tap, I did it myself, and could obtain nothing until I put a lumbar puncture needle in for a depth of three inches. I then got a small amount of gelatinous bloody material, possibly not over two or three cubic centimeters, and then withdrew. I was rather surprised that in view of the x-ray picture and physical findings I did not get a considerable amount of clear fluid.

About her appetite, not only was it unimpaired but she sent out for and ate a large dish of "hot dogs" and potato salad. There is no question about her appetite being good.

The mouth condition, termed thrush, on direct smear showed a very curious large gram-positive bacillus. It cleared up in thirty-eight hours. Clinically the picture could not be distinguished from the type of thrush one sees in infants. As for the filamentous branching organisms, they were present in large numbers in direct smear from the puncture.

Dr. Howard B. Sprague: I saw this patient once in consultation, before much of the laboratory data had been returned, in reference to whether there was a cardiac factor. The thing that impressed me was that the congestion of both upper and lower parts of the body suggested more an obstructive affair than a primary cardiac failure. I thought the most likely thing was either malignancy or an inflammatory process of the right base with probably a metastatic process in the brain.

The electrocardiogram does suggest some decreased myocardial function. I would like to correct one statement about the electrocardiograms; that is, in relation to the T wave in lead four, which is normally inverted in the technique that we use in this laboratory and is commonly used now in this country.

Clinical Diagnosis

Carcinoma of the bronchus.

Dr. Frederick T. Lord's Diagnoses

Arteriosclerosis.
Pneumonitis, actinomycosis or streptothricosis.
Pernicious anemia?
Malignant bronchiogenic carcinoma?

Anatomic Diagnoses

Adenoma of the bronchus.
Multiple abscesses of the lung, right lower lobe.
Pulmonary streptothricosis.
Pulmonary atelectasis, right upper and middle lobes.
Empyema.
Arteriosclerosis, coronary and aortic.
Hypertrophy of the heart.
Secondary anemia.

Pathologic Discussion

Dr. Tracy B. Mallory: The autopsy, unfortunately, was not a complete one. We cannot tell you whether she had anything in the brain. The findings in the chest were as interesting, however, and quite as unexpected as everything else in the clinical course. There was a small empyema. We found that the right lower lobe of the lung was tremendously enlarged, almost completely filling the pleural cavity, and was filled with large multilocular abscesses. On cutting down the bronchi we found just at the bifurcation of the lower lobe bronchus a polypoid tumor which microscopically was perfectly characteristic of a so-called benign adenoma of the bronchus. We have had eight of these benign adenomas preceding this case, all of them heretofore in young patients. The age group in our cases and for the most part in the literature has been a very standard one, running from the late teens to the late twenties, whereas this woman was in the sixties. The question always comes up as to whether they should be considered benign or malignant. The major part of this tumor looks like the typical benign adenomas in young people. It is not encapsulated, however, and the base infiltrates the bronchial wall pretty deeply. Cases of this sort have been described for a good many years as slowly growing carcinomas of the lung, and I would not be surprised at anyone's making that diagnosis on section of this case. On the other hand a very careful search by four members of the department failed to show a single mitotic figure. One wonders if there is any possibility that the tumor may have been present since youth. It seems almost incredible that it could be present all that time without producing symptoms.

The other findings were not of any particular significance. The heart was hypertrophied. There was a moderate degree of coronary sclerosis. The bone marrow was hyperplastic but showed no increase in megaloblasts. Considering the short time she was on liver therapy that allows us to rule out pernicious anemia. The bronchi beyond the tumor were moderately dilated, not markedly so. On microscopic examination of the lungs we have not been able to find any other branching organisms. Very few organisms are visible in the sections. The only ones I have been able to find are evidently cocci, so we must assume that the pulmonary infection was a mixed one.

A Physician: Do you know anything more about the cultures?

Dr. Louis Dienes: The gram-positive fila-

mentous and branching organism which was visible in the pus grew readily on all media. It is an aerobic organism belonging to the group usually called streptothrix. This strain differs in many respects from the actinomyces responsible for most cases of human actinomycosis strains which, as Dr. Lord pointed out, form a well-characterized group. Organisms more or less similar to actinomyces are widely distributed in nature as saprophytes and for all these organisms at present the name actinomyces is used as a generic term. The various strains belonging to the group are regarded as different species of the same genus.

DR. SPRAGUE: Did you find a satisfactory mechanical explanation for venous obstruction in the chest?

DR. MALLORY: No. The increased venous pressure presumably must have been due to some degree of heart failure.

A PHYSICIAN: Was the lower lobe as large as a normal inflated lobe?

DR. MALLORY: Larger, I should say. The other lobe was collapsed and displaced.

A PHYSICIAN: Were the so-called actinomyces artefacts?

DR. MALLORY: I do not believe so. I, myself, saw the smear of the lung puncture and there were unquestionably filamentous organisms in the material. They grew out readily, moreover, in culture.

CASE 22232

PRESENTATION OF CASE

First Admission. A nineteen year old American office boy was admitted complaining of cough and hemoptysis.

Two years before entry after a vague illness of a week's duration, during which he felt slightly feverish and lost his appetite, he suddenly had a paroxysm of coughing associated with a small amount of whitish sputum. A few minutes later he coughed up some bright red blood and returned to his home at once to go to bed. He remained in bed for three days suffering from occasional coughing spells after which he expectorated dark clots and bright red blood. During the three days he brought up about a pint of blood in all. He was told by a physician that he had pneumonia and was sent to a hospital where he remained for three weeks. Sputum and blood examinations and a chest tap were noted as noncontributory. There was occasional blood-streaked sputum during his hospital stay but he had improved markedly at the time of his discharge. There were occasional night sweats and chilly sensations but no further hemoptysis. Eight months after this illness he was confined to bed with "influenza" associated with a cough productive of mucoid, occasionally blood-streaked material. Thereafter he returned to work and except for two occasions, during which he took cold and had some blood-streaked sputum, he remained comparatively well until two months before entry. At this time he developed a sore throat and a cough which was productive of a moderate amount of occasionally blood-streaked yellowish sputum. After ten days he began to expectorate as much as a teaspoonful of bright red blood three or four times daily. He went to bed and remained there until his admission. He had occasional fever, sometimes up to 102°. His appetite flagged but he felt only slightly run down. More recently he controlled his cough voluntarily and the hemoptysis occurred only about once a week, although now it amounted to about a tablespoonful.

Physical examination showed a well-developed but slightly undernourished young man who did not appear acutely ill. The throat was slightly injected and there were several patches of readily removed yellowish exudate. The heart was neither enlarged nor obviously displaced. A soft early systolic murmur was heard at the base. The blood pressure was 140/80. The lungs showed slight impairment of resonance on the left infraclavicular region and diminution of resonance, breath sounds, and tactile fremitus in the postero-inferior portion of the right chest.

The temperature, pulse, and respirations were normal.

Examination of the urine was negative. The blood showed a red cell count of 5,150,000, with a hemoglobin of 75 per cent. The white cell count was 10,400, 91 per cent polymorphonuclears. A sputum specimen was negative for tubercle bacilli and spirochetes. A stool examination was negative. A Hinton test was negative.

X-ray examination showed mottled dullness along the course of the lung markings extending to the right base. In the lateral view the mottling lay in the posterior portion of the lower lobe. After lipiodol injection the left lower bronchial tree was negative. On the right there was obstruction to the passage of the opaque medium down the right lower main bronchus at a point just below the bifurcation of the middle bronchus. At the point of arrest the lower border of the lipiodol had the appearance of a cap formation.

The patient remained quite comfortable during his hospital stay. On the eighth day a bronchoscopy was done. This showed a rounded, red, smooth, shiny mass obstructing the right main bronchus about one quarter of an inch below the lower lip of the upper lobe bronchus. The mass was firm but bled readily at contact with the bronchoscope. No reaction in the surrounding bronchial mucosa was noted. A biopsy showed no definite tumor. Two bron-

choscopies were done at succeeding weekly intervals. Further note was to the effect that the tumor mass was not movable and was quite close to the bifurcation of the right main bronchus. Thereafter the patient received several x-ray treatments to the right chest. He remained quite comfortable and only occasionally had blood-streaked sputum. He was discharged on the forty-sixth day.

Final Admission, two months later.

Following his discharge the patient remained comfortable. A month before re-entry another bronchoscopy showed the tumor to be slightly more hemorrhagic than previously. It now filled almost the entire bronchial lumen. He returned to the hospital for further treatment having had only a single blood-streaked sputum in the interval.

Physical examination was similar to that of the previous admission. A few inspiratory squeaks were heard in the right lower chest posteriorly and the breath sounds were slightly diminished in this region.

The temperature, pulse, and respirations were normal.

Examinations of the blood and urine were negative. Several sputum examinations were negative for blood and tubercle bacilli.

The patient remained comfortable while in the hospital. On the eleventh hospital day an exploratory thoracotomy was done.

Differential Diagnosis

Dr. James H. Townsend: In this case we have hemoptysis coming not out of a clear sky but after a short vague illness of one week's duration, presumably a slight respiratory infection which started him coughing. Then he had hemoptysis. At the age of nineteen certainly in more than ninety per cent of such cases the cause will be found to be tuberculosis. The other small percentage, and presumably in this case we are dealing with that percentage, will be found to belong in another group of rarer conditions which Dr. Lord has just discussed. Among them are tumor (although this is very young for a tumor to cause hemoptysis), rare lung infections such as actinomycosis, a queer sort of pneumonia or possibly the beginning of bronchiectasis or lung abscess. One must also consider the possibility of an unrecognized foreign body. He had a severe coughing fit at the onset of this, but nothing is said about having swallowed anything the wrong way.

I suppose the sputum was negative for tuberculosis, which is to be expected at this stage if it were tuberculosis, and I take it he did have some signs in his chest, presumably the lower part, and they did a chest tap which was negative. What these signs may have been we are not told. At this time we get a suggestion of pus in the sputum which had not been present before.

We are dealing with a situation characterized by a number of brief acute infections, during each one of which cough was a prominent feature and on each occasion there was some blood spitting. On some occasions it was just tiny amounts, but at the first illness there was as much as a pint. At the present illness he is raising considerable quantities of blood, and seems to have more septic involvement. He is now running a temperature and has pus in the sputum as well as blood.

"The throat was slightly injected and there were several patches of readily removed yellowish exudate." I take that to mean that he did have an acute upper respiratory infection. We are not told just where that exudate was, whether on the tonsils or the pharyngeal wall or on the palate. The presence of these patches suggests some unusual sort of throat infection, such as thrush which possibly might get down into the lungs, but on the whole I am not inclined to take these yellowish patches very seriously.

"The lungs showed slight impairment of resonance in the left infraclavicular region and diminution of resonance, breath sounds, and tactile fremitus in the postero-inferior portion of the right chest." In other words some signs reported on both sides of the chest. On the left side the only thing mentioned is slight impairment of resonance in front in the infraclavicular region. I take it that the examiner was looking for evidence of apical pathology. Nothing else was present on that side. I doubt if it has any significance. In the right posterior lower chest there are signs of diminished resonance, diminished breathing, and diminished tactile fremitus. Those are signs suggesting either bronchial obstruction or possibly a small amount of fluid.

We have no mention in this history of pain in his chest and no mention that his cough is related to position.

He had not lost enough blood to make any real difference in his blood picture. The total white count suggests that there was not much infection but there is a very high percentage of polymorphonuclears. He does not seem sick enough though to have the total white count rather low because of an overwhelming infection.

This is all two years after the onset of hemoptysis, and I should think that at this time several negative sputa for tuberculosis are certainly significant and go a long way in ruling out tuberculosis as a cause of his present condition.

The pathology all seems to be in the right lower lobe and the dullness in the left upper lobe apparently was of no significance. Would

you like to comment on the x-rays, Dr. Hampton?

X-ray Interpretation

Dr. Aubrey O. Hampton: This triangular area of dullness occupying the posterior inferior aspect of the right side of the chest is quite typical of a collapse of the lower lobe, and the films taken after lipiodol demonstrate quite clearly the point of obstruction in the right lower lobe bronchus. The inferior margin of the lipiodol shadow shows a concave defect which is often called "cap formation" and is characteristic of a rounded intrinsic mass within the bronchus. There are no other significant findings.

Differential Diagnosis Continued

Dr. Townsend: We have definite evidence that there is obstruction in the right lower main bronchus within an inch or so of the point where the middle bronchus branches from it and the question is what is the nature of the obstruction? The mottling extended into the left base below. This evidently is what one would expect in the way of infection below such an obstruction, doubtless atelectasis and beginning bronchiectasis or abscess formation.

The key to this situation seems to be the bronchoscopic examination. I think this illustrates the importance of making bronchoscopic examinations in all unusual cases of hemoptysis. If this had been done two years previously, possibly the outcome might have been different. There is definite pathology in the right lower bronchus which is described as a tumor mass with very little reaction about it, a mass which bleeds readily, but when they took a specimen from it it showed no definite tumor. I think we can be pretty sure that is not a foreign body. If a foreign body had been there, there would have been much more reaction about it and much more pathology in the lung below it. Moreover, the bronchoscopist visualized the mass and it bled. It presumably is living tissue and the question is the nature of it.

This boy is only nineteen years old. He was seventeen years old at the onset of his illness. He is two years younger than any of the cases of carcinoma of the lung reported by Arkin and Wagner in the *Journal of the American Medical Association*, February 22, 1936. They reported 125 cases, the youngest twenty-one, only three under thirty. This boy was seventeen. Moreover, if it had been malignant to begin with one can hardly conceive that it would not have extended farther or metastasized in the intervening two years. Possibly it may have begun as a benign adenoma and more recently become malignant. There are a number of different tumors that may arise in this region: some may arise directly in the large bronchus and some outside it and extend into it. In this case by x-ray we have no visible evidence of tumor mass outside of the bronchus. This presumably does arise inside and from the bronchial tube itself. Benign adenomata as well as sarcomas occur in this neighborhood, and there is the very rare hemangiosarcoma. The fact that this bleeds so readily suggests that it might belong to that blood vessel tumor type.

Is there any evidence that this might be a metastatic process which has extended into the bronchus? There is none by x-ray. We are not told much about the rest of the physical examination but presumably there was no evidence of any tumor anywhere else in this man's body.

We have three bronchoscopies. I take it that at at least one of these they probably tried to remove this mass but were unable to do so and I would read between the lines that they gave x-ray treatment hoping it might shrink the thing and then after an interval hoped that they might do more. In any case he was out for two months and then came in for his final admission.

"A month before entry another bronchoscopy showed the tumor to be slightly more hemorrhagic than previously." Again a suggestion of very vascular sort of tumor.

"It now filled almost the entire bronchial lumen." Evidently it did not respond to x-ray therapy.

"A few inspiratory squeaks were heard in the right lower chest posteriorly and the breath sounds were slightly diminished in this region." Apparently he still does get considerable air into the right chest.

"Several sputum examinations were negative for blood and tubercle bacilli." Again being sure to rule out tuberculosis. There is no evidence of it.

We have evidence of a definite tumor mass in the right main lower bronchus which has been present for two years at least. We have no evidence of metastases and no definite evidence of a tumor mass in the lung tissue itself from which this arose. On the whole I think it is most likely that this tumor at least started as a benign adenoma or a hemangioma in the bronchial tube, although by this time there may have been malignant changes that developed in the base of it.

He had a thoracotomy presumably because they were unable to remove the lesion by bronchoscopy and they hoped that by a direct approach or approach through the chest wall they might be able to remove it. Dr. Churchill can tell us about that.

Dr. Donald King: I saw this boy before he was admitted to the hospital. My diagnosis was bronchiectasis because we are getting used to seeing the hemorrhagic form of this disease.

Besides hemorrhage this patient also had a story of repeated bronchial infection. After his admission to the hospital the first diagnostic procedure was lipiodol injection. This showed complete obstruction of the right lower lobe bronchus, so that the next step was bronchoscopy and the specimen obtained through the bronchoscope for biopsy showed a benign adenoma which was obstructing the bronchus and had therefore caused bronchiectasis in the obstructed lobe.

We have had altogether eight cases of this so-called benign adenoma of the bronchus. Five of these are living and three have died. Of the three who have died one was given x-ray treatment and had radium seeds implanted in the growth. At autopsy the tumor was still present and the entire lung was destroyed by a suppurative process. The second fatal case died in another hospital after an attempt at bronchoscopic removal of the tumor. The death was said to have been due to novocaine poisoning. The third fatal case is the one presented here today. Of the five living cases one was treated with radium seeds and has done very well, and four have been operated upon. Three of these operative cases have done very well and one is much improved.

The only other point that I wish to make is that repeated bronchoscopic biopsies are often necessary. In one case six bronchoscopic specimens were reported by the pathologists to show only chronic inflammation, and it was not until the seventh specimen was taken that a report of tumor was made.

Clinical Diagnoses

Carcinoma of the lung.
Pericarditis.

Dr. James H. Townsend's Diagnoses

Adenoma of the right primary bronchus, possibly with malignant changes.

Anatomic Diagnoses

(Adenoma of the bronchus.)
Operative wound. Thoracotomy and lobectomy of the right middle and lower lobes.
Pneumothorax, right.
Pleuritis, acute fibrinous, right.
Pericarditis, acute fibrinopurulent.
Acute myocardial degeneration, subpericardial zone.
Myocarditis, fibrous, focal.
Bronchopneumonia, left lower lobe.

Pathologic Discussion

Dr. Edward D. Churchill: The treatment of these cases is an interesting problem. It seems very drastic to attempt a pneumonectomy or lobectomy for a so-called "benign" tumor. By "benign" I mean a tumor which is not given to metastasis or killing by direct extension. These tumors are not benign in the real sense of the word because they eventually do kill the patient. They kill by obstructing the bronchus. Some advanced cases show complete bronchial obstruction, fibrosis and bronchiectasis of the lung leading to a fatal termination. So it is histologically benign, clinically fatal.

The cause of death here, as in the other case, is infection. The inferior pulmonary vein is less than a centimeter in length and in ligating and freeing it a small opening was made into the pericardium. This was sutured but apparently contamination from the bronchial stump was sufficient to produce suppurative pericarditis. He was treated by aspiration and drainage.

This picture is the resected lower and middle lobes. Here is the bronchus and here the polypoid mass in the bronchus. A part of the tumor lies in the lumen of the bronchus and a very considerable proportion lies outside of it. In the majority of these cases the tumor has been confined to the bronchial wall or to the lumen of the bronchus but in this case the tumor had grown beyond the cartilage of the bronchial wall and spread outward a distinct distance into the mediastinum. That is a point of considerable importance from the point of view of therapy. If these tumors could be counted upon to remain entirely within the bronchial lumina they might be treated by bronchoscopic methods with success. Even if one did not succeed in entirely removing the tumor it would be possible from time to time to take off new excrescences as they arose.

Dr. Tracy B. Mallory: This is the first case of so-called adenoma of the bronchus which we have presented at one of these conferences. Although we have now seen nine of them in our own clinic and have also had a chance to review several similar cases from other clinics, the recognition of these tumors as a distinct pathologic entity is a relatively recent event and credit for it is due primarily to the bronchoscopists who recognized the benign character of the lesion before the pathologists did. The first two cases which we had here I called slowly growing adenocarcinoma, as I feel sure the great majority of pathologists have up to the last three years. One of these cases came to autopsy after a five-year course characterized by bronchial obstruction and secondary pulmonary suppuration. The tumor was not encapsulated and showed slight evidences of infiltration at its edges; yet it showed no mitotic figures and after five years of growth was less than an inch in diameter. The second case

was operated upon by Dr. Churchill after a histologic diagnosis of adenocarcinoma from a bronchoscopic biopsy. It was entirely similar histologically. That patient is entirely well today. Shortly after that operation Dr. Churchill called our attention to the reports of similar tumors with a benign clinical course and since that time we have found them relatively easy to recognize if a suitable biopsy specimen can be obtained. Their exact nature is still a matter of controversy and we also do not know whether malignancy can eventually develop.

This patient that we have just discussed today was the third in our entire series. Two bronchoscopic biopsies were reported chronic inflammation, another two were called hemangiomata—a mistake which could easily be made by one unfamiliar with these tumors because of their vascularity, and the last two specimens were finally recognized as adenoma.

The autopsy added comparatively little to our knowledge about this patient. The right pleural cavity showed an acute fibrinous exudate but was free from pus except for a minute pocket immediately beneath the stump of the amputated bronchus and directly overlying the pericardium. The pericardium itself showed an acute fibrinopurulent exudate. Bronchopneumonia had developed in the left lower lobe. Death was undoubtedly due to infection.

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INSTRUCTION IN HOSPITAL ADMINISTRATION

IN spite of the fact that there are about 7,000 hospitals in the United States which, annually, care for 7,000,000 bed-patients and 10,000,000 out-patients, it is only within the past two years that organized instruction in hospital administration has been available. This educational experiment[1] was conceived at the University of Chicago and is being carried out in the School of Business.

For registration, a bachelor's degree or a degree of doctor of medicine or of public health is required. A certain amount of instruction in such fundamental subjects as biology, physiology, economics, sociology, and psychology is required, but, of course, may have been included in the candidate's previous education. The courses cover the medical, community and business aspects of hospital administration, employing classroom and "clinical" methods—the latter consisting of observation and supervised field work in hospitals and clinics. The specific courses vary according to the individual—a medical graduate requiring more training in business methods and students with a business background more training in biology and physiology. This preliminary training, which requires from four to six quarters in the University, is followed by an interneship of six months to one year in a selected hospital. For a master's degree, a thesis must be submitted.

The need for administrative training has been recognized by the American Hospital Association and by the Rockefeller Foundation for many years, and the University of Chicago is to be congratulated for such a courageous and auspicious beginning.

REFERENCE

1. Davis, M. M.: Studies of hospital administration at the University of Chicago. Hospitals **10**:24 (March) 1936.

THE HEALTH ADVANTAGES OF THE UNITED STATES

UNDER the above caption the Metropolitan Life Insurance Company in its statistical bulletin for March, 1936, publishes many interesting comparative figures showing the health advantages which we enjoy over less favored or less enlightened nations.

Cholera and plague are of historical interest to us—there has not been a death from cholera in New York City for forty-three years—but in British India more than 220,000 persons died from cholera, and nearly 46,000 from bubonic plague in the year 1931 alone. In the sixteen states bordering the Atlantic Ocean, where the lesson of vaccination has been well taught, there was only one death from smallpox in 1933; in British India, during the same year, with a population only five times as great, 103,641 smallpox deaths occurred.

The annual typhoid fever mortality in New York and Chicago rarely exceeds one death per 100,000 of population; in Nagasaki, Japan, the death rate from this disease reached 225 per 100,000, in 1931. In La Paz, Bolivia, the 1933 rate was 192 per 100,000, and in Asuncion, Paraguay, it was 187. Delhi, India, registers rates in excess of 100, year after year.

Few of our cities have death rates from measles, scarlet fever, whooping cough or diphtheria in excess of four per 100,000. Bogota, Colombia, Quito, Ecuador, and Karachi, India, register rates of 315, 200 and 175 respectively for measles alone, while La Paz, Bolivia, and San Salvadore, Salvador, record rates of 497 and 159 for whooping cough; the Roumanian cities of Jassy and Bucharest have scarlet fever rates of 59 and 39, and in Kingston-upon-Hull, England, and Ghent, Belgium, diphtheria death rates of 42 and 45 prevail.

In 1918 the death rate from influenza in New York City reached the appalling height of 229 per 100,000 inhabitants; approximately the

same influenza mortality is experienced year after year in Fortaleza, Brazil. The pneumonia death rate in New York has averaged about 100 per 100,000 in recent years. In Madras the annual rate is approximately 700, and in Valparaiso and Manila approximately 500.

Our country-wide tuberculosis mortality has been reduced in thirty-five years to 55 per 100,000, about one quarter of the rate which prevailed in 1900. In Manila the rate is about ten times this figure; in Guayaquil, Ecuador, it is 647; in Callao, Peru, 573; in Lisbon, Portugal, 487, and in Athens, Greece, 414.

Likewise with malaria, although our death rate has increased in recent years to nearly 4 and in some Southern states is as high as 50 and 100, it cannot be compared to Manaos and Belem in Brazil, with their rates of 517 and 407, with Saigon-Cholon in French Indo-China, with its rate of 305, or with San Salvadore, where the rates commonly exceed 225.

Such improvement in public health cannot be attributed to changes in natural conditions or to increased resistance on the part of individuals. The credit is due to the intelligent and tireless efforts of our medical and public health services during the last thirty or forty years.

THIS WEEK'S ISSUE

CONTAINS articles by the following named authors:

HUNTER, FRANCIS T. A.B., A.M., M.D. Harvard University Medical School 1924. Assistant Physician, Massachusetts General Hospital. Associate Physician, Collis P. Huntington Memorial Hospital. His subject is "'Spray X-Ray Therapy' in Polycythemia Vera and in Erythroblastic Anemia." Page 1123. Address: 6 Commonwealth Avenue, Boston, Mass.

HOUSSAY, BERNARDO A. M.D. For information see This Week's Issue, page 946, issue of May 7. His subjects are "The Hypophysis and Resistance to Intoxications, Infections and Tumors" and "Certain Relations Between the Parathyroids, the Hypophysis and the Pancreas." Pages 1128 and 1136. Address: University of Buenos Aires, Buenos Aires, Argentina, S. A.

STERN, ARTHUR. A.B., M.D. Tufts College Medical School 1934. Formerly, Interne, Worcester State Hospital. Now, Interne, Worcester City Hospital. His subject is "Menorrhagia Occurring at the Onset of Catamenia in a Patient with Thrombopenic Purpura: Report of a Case." Page 1147. Address City Hospital, Worcester, Mass.

The Massachusetts Medical Society

SECTION OF DERMATOLOGY AND SYPHILOLOGY

CHANGE IN ANNUAL MEETING PROGRAM

Because of illness it is impossible for Dr. Louis Schwartz of New York to take part in the Annual Meeting Program of this Section. He was to have spoken on Industrial Dermatoses.

In his stead Dr. Marion B. Sulzberger of New York will deliver an address on Definitions and Classifications in Dermatologic Allergy. Dr. Sulzberger is well known for his work on this subject.

MISCELLANY

MAINE NEWS

The Spring Clinic given by the visiting staff of the Eastern Maine General Hospital in conjunction with the Penobscot County Medical Society was held at the hospital on Monday and Tuesday, May 18 and 19, 1936. The discussion was conducted by Dr. C. H. Beecher and Dr. W. T. Rees of Burlington, Vermont.

There were ward rounds in the mornings at 9:30 A.M. and the presentation of cases for discussion in the afternoons at 3:30. The clinic was devoted to general medical and surgical cases. The hospital accepted cases referred to it at no cost for the ward cases other than the regular hospital charges.

On Monday evening, May 18, dinner was served at the Bangor House, following which, Dr. Rees spoke on "Thyroid Disease."

On Tuesday evening, May 19, the Penobscot County Medical Society held its regular meeting at the Nurses' Residence of the Hospital. Following this meeting dinner was served, after which Dr. Beecher discussed "Arteriosclerotic Disease."

Both Dr. Beecher and Dr. Rees are identified with the University of Vermont Medical School, Dr. Beecher being Professor of Medicine and Dr. Rees, Assistant Professor of Surgery.

The Maine Medical Association will hold its Eighty-Fourth Annual Session, June 21-23, 1936, at Rangeley, Maine.

PROGRAM

Conferences

Monday, June 22, 9:30 A.M.

1. Postoperative Abdominal Distention. E. H. Risley, M.D., Waterville.
2. Circulatory Failure in Infectious Disease. R. S. Hawkes, M.D., Portland.
3. Deep Cervical Involvement from Oral and Nasopharyngeal Infections. C. H. Gordon, M.D., Portland.
4. Some Phases of Chronic Uveitis. H. F. Hill, M.D., Waterville.
5. Medical Examiners. G. L. Pratt, M.D., Chairman, Farmington. A round-table discussion.

6. Intrapleural Pneumolysis. G. L. Stivers, M.D., Fall River, Mass.; F. J. Welch, M.D., Portland.

Monday, June 22, 11:00 A.M.

7. Tumors of the Ovary. H. W. Garcelon, M.D., Auburn.
8. Ulcerative Colitis. W. H. Bunker, M.D., Calais.
9. The Necessity for More Thorough Preoperative Study. Wm. Ellingwood, M.D., Rockland.
10. Orthoptic Training. M. C. Moulton, M.D., Bangor.
11. Allergy. J. C. Oram, M.D., South Portland.
12. Fractures. Henry Lamb, M.D., Portland.

Tuesday, June 23, 9:30 A.M.

13. Gallbladder and Gallbladder Duct Surgery. H. L. Robinson, M.D., Bangor.
14. Circulatory Disturbances of the Extremities. J. R. Hamel, M.D., Portland.
15. Chronic Purulent Otitis Media. W. H. Chaffers, M.D., Lewiston.
16. The Malnourished and Nervous Child. A. S. Whittier, M.D., Portland.
17. Medical Treatment in Obstetrics. H. E. Pressey, M.D., Bangor.
18. Early Recognition and Treatment of Mental Disorders by the General Practitioner. C. J. Hedin, M.D., Bangor.

Tuesday, June 23, 11:00 A.M.

19. Acute Abdominal Surgery. J. B. Drummond, M.D., Portland.
20. A Differential Consideration of Precordial Pain. T. E. Hardy, M.D., Waterville.
21. Acute Otitis and Its Complications. C. W. Kinghorn, M.D., Kittery.
22. Digestive Disorders of Infancy and Childhood. A. W. Fellows, M.D., Bangor.
23. The Significance of Bleeding During Pregnancy. L. C. Gross, M.D., Lewiston.
24. Pneumonia. F. A. Winchenbach, M.D., Bath.

Scientific Session

Monday, June 22, 2:00 P.M.

1. Recent Advances in Gastrointestinal Surgery. Wm. Cox, M.D., Lewiston.
2. Office Treatment in Endocervicitis. R. L. Barrett, M.D., New York City.
3. The More Recent Developments in Diabetic Treatment. E. R. Blaisdell, M.D., Portland.
4. Hematuria. C. E. Blaisdell, M.D., Bangor.
5. Maternal Child Health and Crippled Children's Programs Under the Social Security Act. D. A. Murray, M.D., Washington, D. C.

Discussion opened by G. H. Coombs, M.D., Augusta; T. A. Foster, M.D., Portland.

Cancer Symposium

Tuesday, June 23, 2:00 P.M.

Chairman, J. W. Scannell, M.D., Lewiston

Introduction: Cancer in Maine. J. W. Scannell, M.D., Surgeon-in-Chief, Central Maine General Hospital, Lewiston; Chairman, Maine Medical Association Cancer Committee; Chairman, Tumor Clinic, Central Maine General Hospital.

Tumors, Defined and Classified. Julius Gottlieb, M.D., Pathologist, Central Maine General Hospital, Lewiston; Secretary, Maine Medical Association Cancer Committee.

Carcinoma of Breast. Its Early Diagnosis, Prognosis and Treatment. C. M. Robinson, M.D., Chief of Surgical Staff, Maine General Hospital, Portland.

Carcinoma of Pelvis. Routine Examination, Symptoms, Diagnosis and Treatment. M. F. Ridlon, M.D., Surgeon, Eastern Maine General Hospital, Bangor.

Carcinoma of Gastrointestinal Tract. Its Early Symptoms, Diagnosis and Treatment. E. H. Risley, M.D., Surgeon, Thayer Hospital and Sisters' Hospital, Waterville.

Pathology of Carcinoma of Breast, Pelvis and Gastrointestinal Tract. A. H. Morrell, M.D., Director, Diagnostic Laboratory, Augusta.

X-Rays in Diagnosis of Malignant Tumors. F. B. Ames, M.D., Roentgenologist, Eastern Maine General Hospital, Bangor.

Radium Therapy in Treatment of Carcinoma. William Holt, M.D., Surgeon, Maine General Hospital, Portland.

X-Ray Therapy in Treatment of Malignancy. S. A. Wilson, M.D., Roentgenologist, Central Maine General Hospital, Lewiston.

Discussion of Cancer Symposium. Elliott C. Cutler, M.D., Moseley Professor of Surgery, Harvard University Medical School; Surgeon-in-Chief, Peter Bent Brigham Hospital, Boston, Mass. Soma Weiss, M.D., Professor of Medicine, Harvard University Medical School; Physician-in-Chief, Boston City Hospital.

EDWARD H. RISLEY, M.D.

HEALTH OFFICERS' MONTHLY STATEMENT OF VENEREAL DISEASES REPORTED IN NEW ENGLAND FOR MARCH, 1936

State	Syphilis		Gonorrhea	
	Cases Reported During Month	Monthly Case Rates per 10,000 Population	Cases Reported During Month	Monthly Case Rates per 10,000 Population
Connecticut	233	1.41	87	.53
Maine	40	.50	41	.51
Massachusetts	492	1.13	485	1.12
New Hampshire	14	.30	17	.36
Rhode Island	148	2.10	64	.91
Vermont	18	.50	15	.42

—From the Bulletin of the Public Health Service.

A PLEA FOR IMPROVEMENT OF THE SCIENTIFIC PROGRAMS OF COUNTY SOCIETY MEETINGS

The grammar of medicine is an ever-changing body of fundamentals. Whereas in the other learned professions, growth is mainly in the nature of accretion, in medicine growth is more likely to effect a transmutation of basic concepts. This was certainly the case when bacteriology was added to the grammar of medicine. So, too, it was when endocrinology, vitamins and modern psychiatry were discovered and developed. But these transmutations are not invariably effected by epochal discoveries. At times very radical modifications in basic concepts are necessitated by comparatively minor additions to our knowledge. As an instance in point may be taken the recent work on the relation of the physiology of the sympathetic nervous system to such conditions as peptic ulcer and essential hypertension.

The above consideration has a direct bearing upon the education of the doctor, when as a neophyte he acquires it in his school and hospital training, and more particularly on his continued education after graduation and when he is in active practice.

It is often said, half in humor and half in wise deflation, that no one knows so much medicine as the third-year medical student. His knowledge is so pat, so precise! He "knows the answers," that is, provided he is a good book student. It will require some years of experience and an impressive accumulation of failures to free the young doctor of his conceit. He will only slowly learn the lesson that "grammar" is a body of tools, and that art is still elusive. It is a pity then that the young man is not spared the delusion, and that what is taught him is not served with a warning on its tentative nature, and with the advice that not only is it subject to change, but that indeed periodic change and reinterpretation will be essential to his continued professional growth.

While there are many concerned with the curricula of medical schools, the situation is otherwise with what is termed graduate education. Training for specialization has been accorded a measure of study. But such instruction embraces only a small portion of the medical personnel. Most doctors are, and will continue to be, general practitioners. They too may periodically desire specialty training, as their practice leans heavily in the direction say of obstetrics, gynecology, surgery, and so forth. But here our concern is with general instruction for the general practitioner, in general medicine. This is necessitated for every man by what we term rather loosely "the advances in medicine," but which, as we indicated above, arises out of the labile nature of the grammar of our science.

For this type of instruction we can hardly provide formal schooling. There is no fixed curriculum, no defined teaching body. Here we need a means so that "he who runs may read" or, more fittingly, so that he who is in active practice may bring his knowledge up to the mark without withdrawing from everyday activity. The need for this type of instruction has not gone unrecognized. Indeed, many county associations and academies have organized lecture series for the general practitioner. In the New York Academy of Medicine, to cite but one illustration, Friday afternoon lectures are available for the practitioners of the metropolis and, during the last eight years, a Graduate Fortnight, devoted to some one but embracive division of medical practice, has been held. These are unique teaching activities, as one can readily gather from the programs. They are not devoted primarily to what is the newest, the most recent and the least tried of medical ideas and practices; they are rather résumés of what is known, what is accepted and what has been proved. They are a consolidation of thought and advance in our science.

But even these unique teaching endeavors can reach only a small percentage of our profession. To render the practice more widespread and hence more fruitful, the concept must be instilled into that forum called the county society meeting. Here we have the most numerous and most common meeting place and occasion where and when doctors foregather. The county society meeting should, therefore, offer the very best opportunity for this desirable form of instruction.

Our medical journals as a group should prove no less valuable a medium for such education, but here we touch on a rather complicated subject and one which we can at this time no more than touch.

Let us apply ourselves more closely to the problem. We grant that the recently graduated physician is a rather raw product. If he continues for ten years without learning more than he knew when he came out of medical school and if he does not readjust his viewpoint, his philosophical concepts, so to say, he will find himself badly behind the procession. How then does he, or how should he, continue his education? Of course, he may take graduate instruction in some specialty or in internal medicine. While this is increasingly the practice among the younger men, the number is still very small, and it is difficult for the older man who must stay on the job.

Of course he can read his medical journals, but most of the journals haven't yet "gotten the idea." Their columns are filled with the newest hypotheses, the rare cases and the highly intricate conditions. True, occasionally one finds in an annual address or in a contribution by some outstanding scholar an excellent résumé of a given field or subject. In such instances this precious material is usually presented in the historical introduction, which, as likely as not, will be skipped by the reader, since most "histories" are merely an uncritical recitation of names and dates.

To give due credit we must, however, note that the *Journal of the American Medical Association* has in recent months published excellent résumés on therapy and on endocrinology. Also the *Lancet* has been publishing serial résumé articles. These, valu-

able though they be, are too infrequent and loom small in the bulk of published material.

And finally, not all medical men are, so to say, eye-minded. Some cannot gain much from the printed page or find the effort too taxing and unprofitable. For them, the human voice is more effective and a more productive medium. The hospital conference, contact with fellow practitioners and meetings, serve best as sources of instruction for a large number of doctors.

This argues, then, for making the county society meeting truly instructive by offering, periodically, résumé programs. This idea is a simple one. Alas, too fatally simple. For, if it is applied crudely, uncritically, it creates a pathetic effect. What can be more boring than being told what is all too well known? Hash is hash, even when called a résumé. But we are not after hash in the résumé meeting. We need and desire a recrystallization of thought and knowledge in a given field, a rearrangement of old elements to make a new pattern, a trimming of dead limbs to bring new life into a branch of knowledge. All of which calls for the choice of a suitable subject and a competent essayist.

There is a time and seasonableness for subjects. Not all may be revalued effectively; in many there is nothing new to report, as the old concepts still hold good. But others cry for restatement. There is a sort of nodal point at which progress in a given field may be focused to form a new and clear picture. Such is the instance now in the diseases of the blood, and in the evaluation of the emotional factor in functional disturbance. A year from now the time may be ripe for a résumé of physical therapy in general practice. Nutrition, the diagnosis and treatment of tuberculosis and traumatic surgery are fit subjects for restatement.

But one cannot readily compose a catalogue and schedule of subjects to be so treated which are suitable for differing times and places. The task is not for one man and the problem varies from place to place. But the essential idea is important. A résumé is not a mere restatement of what is known. It is essentially a philosophical task, it is the bringing forth of a new concept, at times furthering, at times reversing, the older concept. It is a critical evaluation, a sifting of older knowledge and its amalgamation with newer knowledge. A résumé is, indeed, of the very nature of the philosophy of medicine, that phase of medicine which is as precious as its science.

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2 E. 103rd Street, New York City.

PATENT MEDICINES SEIZED BY FEDERAL INSPECTORS

Patent medicines are conspicuously present in the U. S. Department of Agriculture report of May 25, 1936. The products seized, their compositions, and the curative claims alleged to be false and fraudulent, are as follows:

"Anti-Itch," a petrolatum ointment containing zinc oxide, glycerol, wintergreen and carbolic acid (10.63 per cent). The product was also held to be misbranded under the Federal Caustic Poison Act since it had no label statement of the common name of the poison it contained, no "Poison" warning, and no antidote in case of accidental injury.

"Booth's Hyomei," a solution of eucalyptol, menthol and creosote in alcohol and water, for catarrh, hay fever, catarrhal coughs, croup, bronchitis, catarrhal laryngitis, lung affections and difficult breathing (the product was further misbranded in declaring an alcohol content of 12 per cent when it contained only 9 per cent, and in representing its vapors as antiseptic.

"Bralot Rheumatic Tablets," containing amidopyrine, sodium salicylate, and coated with chocolate, for rheumatism, gout, neuralgia, neuritis and sciatica.

"Diaplex," consisting of the dried leaves and stems of the salt bush, for diabetes.

"Four Leaf Clovers," pink tablets containing boric acid, borax and starch, falsely represented as antiseptic, and for various ailments of women.

"G. S. Alterative Tonic," a solution of plant drugs and potassium iodide in alcohol and water, for pellagra, rheumatism, liver and kidney ailments, and as a tonic.

"H.P. Antiseptic and Healing Balm," a lead oleate ointment not antiseptic as represented, and claimed safe despite its lead content, for a multitude of lesions.

"Hi-Test Catarrhal Jelly," a deteriorated salvage drug containing petrolatum, menthol and eucalyptol, for catarrh and hay fever; "Kopp's," a syrup containing the narcotic morphine sulphate, represented as safe for children.

"Lacta Kaolin Alpha," consisting of lactose, kaolin (clay), agar and cocoa, represented as a food, although composed chiefly of nonfood ingredients; "Lacta-Kaolin Laxative," of the same composition as the preceding product, with the addition of the coal-tar laxative phenolphthalein, without reference to the presence of the laxative drug.

"Mentos," a water solution of sulphur, borax, ammonia and perfume, represented as antiseptic but found on test incapable of killing pathogenic organisms.

"Mother Beach Stomach Tablets," made of sodium bicarbonate, bismuth subnitrate and magnesium oxide, for stomach ulcers, indigestion, and other ailments.

"My-Kel Tooth Powder," sodium perborate and talc, flavored with wintergreen, for keeping the gums firm, building up the tooth enamel, for pyorrhea, and to maintain freedom from mouth infections.

"Quality Sealed Sore Throat Remedy," another deteriorated salvage drug, a solution of potassium chlorate, tannic and carbolic acid in glycerin and water, short of the declared volume, for sore throat.

"Tricasco," a solution of plant extracts, licorice, a laxative and sugar, for forty ailments including consumption, pneumonia, rheumatism, palpitation of

the heart, gout, gallstones and stomach ulcers.

"Ward's Vitamized Tonic Tablets," containing iron, iodine, calcium, a fish liver oil and berberine, making claims of vitamin A and D potency that were found on test to be unsupportable.

THE CONTROL OF SILICOSIS BY THE U. S. DEPARTMENT OF LABOR

Secretary of Labor Frances Perkins has announced the appointment of four committees, specified below, in the co-operative campaign to lessen the ravages of silicosis to which 500,000 workers in mines, quarries, foundries, glass works and other industries where silica dust may be inhaled are exposed in some degree.

COMMITTEE ON THE PREVENTION OF SILICOSIS THROUGH MEDICAL CONTROL

Chairman — Surgeon R. R. Sayers, U. S. Public Health Service, Washington, D. C.; L. U. Gardner, M.D., Director, Saranac Laboratories, Saranac Lake, N. Y.; Wesley M. Graff, National Bureau of Casualty and Surety Underwriters, New York City; Thomas Kennedy, United Mine Workers of America, Harrisburg, Pa.; A. J. Lanza, M.D., Metropolitan Life Insurance Company., New York City; W. S. McCann, M.D., Strong Memorial Hospital, Rochester, N. Y.; E. P. Pendergrass, M.D., University of Pennsylvania, Philadelphia, Pa.; B. L. Vosburgh, M.D., National Electrical Manufacturers Association, Schenectady, N. Y.; C. H. Watson, M.D., President, National Safety Council, New York City; J. Norman White, M.D., Scranton, Pa.

COMMITTEE ON THE PREVENTION OF SILICOSIS THROUGH ENGINEERING CONTROL

Chairman—Warren A. Cook, State Department of Health, Hartford, Conn.; Cyril Ainsworth, American Standards Association, New York City; James R. Allan, International Harvester Company, Chicago, Ill.; J. J. Bloomfield, U. S. Public Health Service, Washington, D. C.; Thomas G. Donnelly, State Federation of Labor, Columbus, Ohio; Professor Philip Drinker, Harvard School of Public Health, Boston, Mass.; C. H. Fry, Chief, Bureau of Industrial Accident Prevention, Department of Industrial Relations, San Francisco, Calif.; Leonard Greenburg, M.D., Division of Industrial Hygiene, New York State Department of Labor, New York City; Daniel Harrington, U. S. Bureau of Mines, Washington, D. C.; Willis G. Hazard, Owens-Illinois Glass Company, Toledo, Ohio; E. O. Jones, American Foundrymen's Association, Chicago, Ill.; E. G. Meiter, Employees' Mutual Liability Company, Milwaukee, Wis.; W. P. Yant, Supervising Engineer, U. S. Bureau of Mines Experiment Station, Pittsburgh, Pa.

COMMITTEE ON ECONOMIC, LEGAL, AND INSURANCE PHASES OF THE SILICOSIS PROBLEM

Chairman—V. P. Ahearn, National Sand and Gravel Association, Washington, D. C.; Daniel D. Carmell, Assistant Attorney-General, Chicago, Ill.; J. Dewey Dorsett, Industrial Commission, Raleigh, N. C.; Evan I. Evans, Supervisor, Actuarial Division, Ohio Industrial Commission, Columbus, Ohio; John P. Frey, American Federation of Labor, Washington, D. C.; Henry D. Kessler, M.D., Chairman, Rehabilitation Commission, Newark, N. J.; Voyta Wrabetz, Chairman, Wisconsin Industrial Commission, Madison, Wis.; Louis B. Raycroft, Pennsylvania Self-Insurers, Philadelphia, Pa.; Henry D. Sayer, Association of Casualty and Surety Executives, New York City; T. C. Waters, Chairman, Maryland Occupational Disease Commission, Baltimore, Md.; Robert J. Watt, Massachusetts Federation of Labor, Boston, Mass.; David S. Beyer, Liberty Mutual Insurance Company, Boston, Mass.; W. H. Winans, Union Carbide and Carbon Corporation, New York City; William F. Roeber, National Council of Compensation Insurance, New York City.

COMMITTEE ON REGULATORY AND ADMINISTRATIVE PHASES OF THE SILICOSIS PROBLEM

Chairman—L. Metcalfe Walling, Labor Commissioner, Providence, R. I.; Leon S. Senior, Compensation Insurance Rating Board, New York City; P. G. Agnew, M.D., American Standards Association, New York City; Dan Boney, Insurance Commissioner, Raleigh, N. C.; Manfred Bowditch, Director, Bureau of Occupational Hygiene, Boston, Mass.; Joseph A. Haller, Safety Engineer, Compensation Commission, Baltimore, Md.; Ambrose B. Kelly, American Mutual Alliance, Chicago, Ill.; Michael J. Murphy, Director, Workmen's Compensation, New York City; Victor A. Olander, Secretary, Illinois Federation of Labor, Chicago, Ill.; Stanley Osborn, M.D., Health Commissioner, Hartford, Conn.; W. C. Woodward, M.D., American Medical Association, Chicago, Ill.; J. H. Oliver, Glen Alden Coal Company, Scranton, Pa.; Martin P. Durkin, Director, Illinois Department of Labor, Chicago, Ill.; R. M. Hartman, Assistant Secretary, Workmen's Compensation Department, Charleston, W. Va.

RECENT PUBLICATIONS OF THE METROPOLITAN LIFE INSURANCE COMPANY

A series of pamphlets for lay readers has been prepared by the Metropolitan Life Insurance Company. The titles of these brochures are as follows:

Taking Your Bearings — Emphasizes the value of periodical physical examinations, at various ages. The old seaman on the cover shooting the sun with a sextant gives the keynote to the pamphlet. Just as a seaman uses his nautical instruments to locate danger spots, so with the help of a physician's knowledge and special instruments, one can discover and avoid many of the physical hazards of life.

Care of the Eyes—Outlines practical methods of conserving eyesight and describes in simple language the more common eye defects and eye diseases.

Sleep—Deals with the importance of sleep, rest, and relaxation for all ages, emphasizing their close relationship to health and disposition. Points out that how well we sleep is as important as how long

we sleep. Includes definite sleeping instructions for children.

Calling All Drivers — Discusses such topics as—What speed is too fast? When your car skids. How to meet emergencies. Know your signals. Appropriate for individuals and for use in organized safety campaigns.

Infantile Paralysis — Recent developments in infantile paralysis research made it necessary for us to revise our leaflet. The revised pamphlet is edition (g) 353 L.W. If you have any other editions on hand they should be destroyed.

The Baby — Birth to one year. New cover and slight revision of text.

For Good Health — Food poster 22 by 28 inches. Although published almost two years ago, it is still useful in calling attention to adequate food allowances.

In line with our regular distribution policy, we shall be glad to supply limited quantities of these pamphlets to accepted health and social agencies. They should be ordered direct from the Welfare Division.

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR APRIL, 1936

Disease	Apr., 1936	Apr., 1935	5 Yr. Average*
Anterior Poliomyelitis	2	1	2
Chickenpox	895	1,081	1,059
Diphtheria	23	25	94
Dog Bite	890	1,103	543
Epidemic Cerebrospinal Meningitis	28	9	9
German Measles	644	8,695	1,917
Gonorrhea	486	508	466
Lobar Pneumonia	551	539	504
Measles	5,569	2,157	3,478
Mumps	2,174	486	795
Scarlet Fever	1,217	1,028	1,498
Syphilis	514	498	393
Tuberculosis, Pulmonary	314	293	322
Tuberculosis, Other Forms	34	29	40
Typhoid Fever	1	13	10
Undulant Fever	3	6	—
Whooping Cough	363	522	905

*Based on the figures for the preceding five years.

RARE DISEASES

Anterior poliomyelitis was reported from Attleboro, 1; Wellesley, 1; total, 2.

Anthrax was reported from Haverhill, 1.

Diphtheria was reported from Arlington, 1; Boston, 5; Fall River, 3; Framingham, 1; Lowell, 4; Lynnfield, 4; Medford, 1; Montague, 1; Somerville, 1; Wilmington, 1; Worcester, 1; total, 23.

Dysentery, amebic was reported from Cambridge, 1.

Encephalitis lethargica was reported from Newton, 1; Worcester, 1; total, 2.

Epidemic cerebrospinal meningitis was reported from Amherst, 1; Athol, 1; Boston, 10; Bridgewater, 2; Brockton, 1; Deerfield, 1; Hopedale, 1; Lynn, 1; Millbury, 1; New Bedford, 1; Natick, 1; Saugus, 1; Somerset, 1; Somerville, 1; Tewksbury, State Infirmary, 1; Wendell, 1; West Springfield, 1; Worcester, 1; total, 28.

Hookworm was reported from Quincy, 1.

Malaria was reported from Boston, 1.

Septic sore throat was reported from Boston, 9; Brookline, 2; Easthampton, 1; Gardner, 9; Lynn, 1; Medford, 1; Somerville, 2; West Brookfield, 4; total, 29.

Tetanus was reported from Boston, 1.

Trachoma was reported from Worcester. 1.

Trichinosis was reported from Springfield, 1.

Typhoid fever was reported from Waltham, 1.

Undulant fever was reported from Barnstable, 1; Norton, 1; Winchendon, 1; total, 3.

There was less diphtheria reported throughout the month than for one week of the corresponding month in 1932.

To date typhoid fever morbidity is running slightly below last year's record low figure.

The incidence of epidemic cerebrospinal meningitis continues at a higher level than usual with practically all sections of the State represented.

Although pulmonary tuberculosis morbidity showed a slight increase over April of last year, the reported deaths through March showed a considerable decrease.

The reporting of anterior poliomyelitis, chickenpox, and tuberculosis other forms was not remarkable.

The reported incidence of whooping cough remained lower than at any time since 1917.

Mumps continued to be reported to the highest level in the history of the State.

Scarlet fever, although reported slightly above the figures for the previous two years, remained well below the five-year average.

German measles morbidity apparently reached its peak in March, although usually this occurs in May.

Measles still continues epidemic in a number of eastern communities, particularly the metropolitan area and Worcester.

EXTRACT FROM A REPORT OF THE JULIUS ROSENWALD FUND

During the past year plans for making medical care more available to people of small means have grown substantially. Voluntary insurance to lower the cost of hospital care — group hospitalization—has doubled now covering some 350,000 persons with plans being established monthly in new communities. A recent publication of the Fund described new plans for securing general medical care on a group payment or insurance basis, conducted in many parts of the United States by industrial agencies, co-operative societies, groups of physicians and medical societies and benefiting several million people. The Fund will continue to assist in the exten-

sion of the insurance principle in relation to hospital service, in scientific studies concerning the cost and the organization of medical care and in the education of qualified personnel for studying and administering hospitals and clinics.

MORTALITY RATES

Telegraphic returns from 86 cities with a total population of thirty-seven millions for the week ending May 9, indicate a mortality rate of 12.6 as against a rate of 12.0 for the corresponding week of last year. The highest rate (21.5) appears for Tacoma, Wash., and the lowest (4.1) for Waterbury, Conn. The highest infant mortality rate (13.1) appears for San Antonio, Texas, and the lowest for Erie, Pa., Fall River, Mass., Fort Wayne, Ind., Grand Rapids, Mich., Hartford, Conn., San Diego, Calif., Schenectady, N. Y., Somerville, Mass., and South Bend, Ind., which reported no infant mortality.

The annual rate for 86 cities is 13.5 for the nineteen weeks of 1936, as against a rate of 12.6 for the corresponding period of the previous year.

SUMMARY OF DEATHS AND DEATH RATES (ANNUAL BASIS) FROM AUTOMOBILE ACCIDENTS PER 100,000 ESTIMATED POPULATION FOR 86 CITIES FOR CORRESPONDING PERIODS OF 1936 AND 1935

	Week ending		First 19 weeks	
	May 9, 1936	May 11, 1935	1936	1935
Total deaths	163	161	2,665	3,110
Death rate	22.8	22.4	19.6	22.8
Deaths due to accidents in city	131	131	2,067	2,529
Death rate	18.3	18.3	15.2	18.5

—*Bulletin, Bureau of the Census.*

THE RESIGNATION OF DR. DAVID D. SCANNELL

DR. David D. Scannell has resigned as Surgeon-in-Chief of the Boston City Hospital, effective June 1, 1936.

THE RECORD FOR BLOOD TRANSFUSIONS

Raymond Briez of Paris holds the record for blood transfusions, having supplied 98 in one year. Since 1924 he has sold 257 quarts of his blood, without suffering any ill effects. — *Bulletin*, New York State Medical Society.

THE THREE CENTS A DAY HOSPITAL PLAN

A prediction made at the meeting of the Hospital Association of the State of New York at Buffalo, May 22, 1936, is to the effect that the "three cents a day hospital plan" will be popular in the larger cities of New York State.

It was asserted that 33,000 persons in Rochester, New York and 90,000 in New York City have subscribed to the plan.

It involves neither charity nor profit, according to Mr. Frank Van Dyk, Executive Director of the Associated Hospital Service of New York City.

RECENT DEATHS

UPTON—CHARLES LOUIS UPTON, M.D., whose office was at 31 Federal Street, Greenfield, Massachusetts, died May 25, 1936. Dr. Upton was born at Shelburne Falls in 1870, the son of Oliver and Sarah (Duncan) Upton and after a preliminary education at Arms Academy and Amherst College, he matriculated at the University of Pennsylvania School of Medicine and graduated in 1896. Soon afterward he settled in Shelburne Falls where he practiced until he moved to Greenfield in 1925.

Dr. Upton was a Fellow of the Massachusetts Medical Society and the American Medical Association and a member of Lieutenant John J. Galvin Post of the American Legion.

His widow, a son, Duncan G. Upton, and a daughter, Mrs. Ruth Chase and four grandchildren survive him.

HART—MICHAEL JOSEPH HART, M.D., of 1635 Dorchester Avenue, Boston, died at the Boston City Hospital, May 23, 1936.

Dr. Hart was born in Fitchburg, Massachusetts, in 1871 and was a graduate of Boston College, and of the Medical School of Harvard University, class of 1896. He practiced in Ashmont for about forty years.

Dr. Hart was not married. Five nieces, Mrs. George J. Weldon, Mrs. David Drinkwine, Mrs. W. F. O'Brien, Mrs. Raymond T. Powers, and Mrs. William G. Hay, and two nephews, Paul F. and John J. McElroy, all of Fitchburg, survive him.

NOTICES

AN AWARD OF ONE THOUSAND DOLLARS FOR A MANUSCRIPT ON A SCIENCE SUBJECT

A cash award of $1000 is offered by The Williams & Wilkins Company for the best manuscript on a science subject, presented before July 1, 1937.

Literary prizes are relatively common, but it is not so usual for a publisher to be bidding for science material in this manner.

The publishers put no limitations on the subject-matter or manner of handling, and none on eligibility for the award. The MS. must be in English and "of a sort calculated to appeal to the taste of the public at large." The desired length is given as 100,000 words.

While any MS. on a science subject will be considered, it is expected that the author will prove to be a man or woman engaged in a scientific pursuit who is possessed of the requisite literary skill to interpret science for that portion of the public which reads books.

To assure authenticity, the publishers have enlisted the services of some twenty-five or thirty "advisers," these being men of science of wide reputation and assured competence. One or more of the advisers will pass upon each MS. from the viewpoint of soundness and accuracy.

The award will lie in the joint discretion of four judges selected with a view to their especial qualification in choosing the sort of book that will appeal. These are the following: Dr. Joseph Wheeler, Librarian of the Pratt Library in Baltimore, and chairman of the Book List Committee of the Association for the Advancement of Science; Harry Hansen, reviewer and critic for the *New York World Telegram* and *Harpers Magazine;* Dr. Lyman Bryson, Professor of Education of Teachers College, Columbia, and Director of the "Readability Laboratory," and David Dietz, science editor of the Scripps-Howard newspapers.

Further details concerning the award may be had by addressing the publishers at Mt. Royal and Guilford Avenues, Baltimore, Maryland.

HARVARD UNIVERSITY TERCENTENARY CELEBRATION 1636-1936

Symposium on the Environment and Its Effect upon Man

August 24 to 29, 1936, at the School of Public Health, 55 Shattuck Street, Boston

Monday

9:30 A.M. The Effects of the Social Environment. Dr. Lawrence J. Henderson, Abbot and James Lawrence Professor of Chemistry, Harvard University and Dr. Elton Mayo, Professor of Industrial Research, Harvard Business School.

11:00 A.M. Fatigue. Dr. David B. Dill, Assistant Professor of Biological Chemistry, Harvard School of Public Health.

2:00 P.M. Air-borne Disease. Dr. Wilson G. Smillie, Professor of Public Health Administration, Harvard School of Public Health.

3:30 P.M. Bacteria and Pollen in Air. Mr. William F. Wells, Instructor in Sanitary Science, Harvard School of Public Health.

8:00 P.M. Reception to members of the Symposium and their families.

Tuesday

9:30 A.M. The Physiological Effects of High Temperatures and Humidities. Dr. Cecil K. Drinker, Professor of Physiology and Dean, Harvard School of Public Health.

11:00 A.M. Industrial Air Conditioning. Mr. Constantin P. Yaglou, Assistant Professor of Industrial Hygiene, Harvard School of Public Health.

2:00 P.M. The Physiological Effects of High Pressures. Mr. Louis A. Shaw, Assistant Professor of Physiology, Harvard School of Public Health.

3:30 P.M. Industrial Operations in Compressed Air. Mr. Ole Singstad, Chief Consulting Engineer on Tunnels, Port of New York Authority.

Wednesday

9:30 A.M. Carbon Monoxide Poisoning. Dr. Cecil K. Drinker.

11:00 A.M. Occurrence and Significance of Gaseous Impurities. Mr. William P. Yant, Supervising Chemist, Health Laboratory Section and Supervising Engineer, Pittsburgh Experiment Station, U. S. Bureau of Mines.

2:00 P.M. The Toxicology of Organic Vapors and Gases. Dr. John S. Foulger, Haskell Laboratory of Industrial Toxicology, Wilmington, Del.

3:30 P.M. The Toxic Dusts. Dr. Lawrence T. Fairhall, Assistant Professor of Physiology, Harvard School of Public Health.

Thursday—Pneumoconioses

9:30 A.M. Causation. Mr. Philip Drinker, Professor of Industrial Hygiene, Harvard School of Public Health.

11:00 A.M. Clinical Aspects, Diagnoses, Prevention. Dr. W. Irving Clark, Physician to The Norton Company and Assistant Professor of the Practice of Industrial Medicine, Harvard School of Public Health.

2:00 P.M. Control. Mr. Theodore F. Hatch, Instructor in Industrial Sanitation, Harvard Schools of Engineering and of Public Health.

3:30 P.M. Protective Equipment. Dr. Carlton E. Brown, Chemist, Gas Section, Pittsburgh Experiment Station, U. S. Bureau of Mines.

Friday

9:30 A.M. The Application of Air Conditioning in Normal Life. Mr. Philip Drinker.

11:00 A.M. The Application of Air Conditioning to Hospitals. Mr. C. P. Yaglou.

2:00 P.M. A Laboratory of Industrial Toxicology. Dr. W. F. von Oettingen, Director, Haskell Laboratory of Industrial Toxicology, Wilmington, Del.

3:30 P.M. A Laboratory of Industrial Hygiene. Mr. Warren F. Cook, Chief Industrial Hygienist, State Department of Health, Hartford, Conn.

Saturday A.M.

Demonstration in the Harvard School of Public Health and visits to the Industrial Clinic, The Norton Company, Worcester, Mass.; The Fletcher Granite Company, West Chelmsford, Mass.; The Fatigue Laboratory, Harvard Business School.

To cover the expenses of the symposium a fee of $25 will be charged those who attend. For further information address Marian Dale, Secretary, 55 Shattuck Street, Boston, Mass.

TERCENTENARY SESSION OF THE HARVARD MEDICAL SCHOOL

September 14 and 15, 1936

As part of the University celebration, the Medical School and the Medical Alumni Association invite the graduates of the School to return on September 14 and 15 for the Medical School Exercises

and Medical Alumni Reunion. These will immediately precede the final Cambridge exercises on September 16, 17 and 18.

The Medical School Exercises will include:

Demonstrations, special clinics, discussions and exhibits at the various hospitals associated with the Harvard Medical School.

Four carefully planned symposia programs, presented by the Harvard Medical Faculty, on

Nutrition and the Deficiency Diseases
Chairman, Dr. George R. Minot

The Nervous System; Central and Sympathetic
Chairman, Dr. Walter B. Cannon

The Infectious Diseases
Chairman, Dr. Hans Zinsser

The Endocrine Glands
Chairman, Dr. J. Howard Means

The annual meeting and the dinner of the Harvard Medical Alumni Association will be held on the evening of September 15 in Vanderbilt Hall. This meeting has been postponed from its usual time in June in honor of the Tercentenary and to encourage the return at this time of as many graduates as possible.

"Open House"

July, August and September

The Tercentenary Celebration begins on July 6, 1936, when the University places its various buildings and activities "on view." Most of the departments of the Medical School and the affiliated hospitals will keep "open house" for all or part of the summer. During this time one or more members of the staff of each department will always be available to receive returning graduates or interested visitors, and show and explain the routine activities or such demonstrations and exhibits as the department may offer. Further information as to items of special interest, dates and times will be published in the Medical Alumni Bulletin, and will be available during the summer at the Tercentenary Office in Cambridge.

Program of the Tercentenary Session of the Medical School

Monday, September 14

9:00 A.M.-12:30 P.M. Clinics and demonstrations

The "open house" demonstrations and exhibits of the summer will be continued during this morning. The members of the staffs will be present to discuss their work informally, and many of the departments and hospitals will offer special clinics and demonstrations. The full program will be announced at a later date in the Medical Alumni Bulletin.

12:30 P.M. Buffet luncheon in Vanderbilt Hall

2:00-5:00 P.M. Harvard Medical School, Building D:

Introduction to the Symposia

Dr. David L. Edsall, Dean Emeritus

Nutrition and the Deficiency Diseases

Chairman: Dr. George R. Minot

Dr. J. L. Gamble — Intracellular Fluid and Its Maintenance
Dr. C. M. Jones—Protein Deficiency
Dr. C. W. Heath—The Deficiencies of Circulating Hemoglobin
Dr. W. B. Castle—The Relationship of Defective Nutrition to Changes in the Gastro-Intestinal tract
Dr. S. B. Wolbach—Vitamin C and the Formation of Intracellular Material
Dr. K. D. Blackfan — Sub-Optimal Nutritional States and Partial Vitamin Deficiency
Dr. P. Howe — Oral Pathology in Relation to Avitaminosis
Dr. M. B. Strauss—Nerve Disorders Arising from Defective Nutrition
Dr. E. P. Joslin—Present Aspects of Diabetes

Monday evening is held open for possible Medical class reunions and hospital reunions.

Tuesday, September 15

There will be two simultaneous sessions on Tuesday morning

(A) 9:30 A.M.-12:30 P.M. Harvard Medical School Building C:

The Nervous System; Central and Sympathetic

Chairman: Dr. Walter B. Cannon

Dr. J. C. White — Surgery of the Sympathetic Nervous System
Dr. A. Rosenblueth — Chemical Mediation of Nervous Effects
Dr. J. B. Ayer — The Use of Prostigmine in Myasthenia Gravis
Dr. H. Davis — The Electrical Activity of the Human Brain
Drs. F. A. Gibbs and W. G. Lennox—The Electrical Activity of the Brain in Epilepsy
Dr. S. Cobb—Cerebral Circulation
Dr. S. Weiss—Syncope and Collapse
Dr. T. J. Putnam—The Pathogenesis of Multiple Sclerosis

(B) 9:30 A.M.-12:30 P.M. Harvard Medical School, Building D:

The Infectious Diseases

Chairman: Dr. Hans Zinsser

Dr. Hans Zinsser—Recent Advances in the Study of Typhus Fever
Dr. C. F. McKhann—The Immunological Application of Placental Extract
Dr. W. G. Smillie—Epidemiological Studies on the Virus of Influenza
Drs. C. S. Keefer and W. W. Spink—Immune Reactions in Gonococcal Infections
Dr. A. W. Sellards—Yellow Fever

Dr. C. Lyons — Antibacterial Immunity in Hemolytic Streptococcic Infections

Dr. E. S. A. Robinson—The Antiserum Treatment of Pneumonia from the Standpoint of Public Health

Dr. M. Finland—Some Aspects of Pneumococcus Infection in Man

Dr. R. P. Strong—Studies on Filarioidea

Dr. D. L. Augustine—Trichinosis; Incidence and Diagnostic Tests

Drs. H. Pinkerton and G. M. Hass—Cultivation of Rickettsia in Tissue Culture

12:30 P.M. Buffet luncheon in Vanderbilt Hall

2:00-5:00 P.M. Harvard Medical School, Building D:

The Endocrine Glands

Chairman: Dr. J. Howard Means

Dr. G. B. Wislocki — The Blood Supply to the Hypophysis

Dr. H. B. Friedgood—The Nervous Control of the Anterior Hypophysis

Dr. E. C. Cutler—Diabetes Insipidus: Its Relation to Hypophysis and Thyroid

Dr. J. C. Aub — Hypophyseal-Parathyroid Relationships

Dr. A. B. Hastings—Factors Governing the Calcium Equilibria of the Body

Dr. F. Albright—The Action of the Parathyroid Hormone upon the Skeleton

Dr. E. D. Churchill—The Surgery of the Parathyroids

Dr. W. T. Salter—The Genesis of Thyroid Protein

6:00 P.M. Annual Meeting of the Medical Alumni Association

7:00 P.M. Dinner of the Alumni Association in Vanderbilt Hall

REPORTS AND NOTICES OF MEETINGS

THE BOSTON UNIVERSITY SCHOOL OF MEDICINE ALUMNI

Describing the relationship of mental factors and disease to illness and the fact that psychiatry is in close touch with many community activities, Dr. Winfred Overholser, State Commissioner of Mental Diseases, in an address delivered recently before the annual gathering of the Boston University School of Medicine Alumni at the Hotel Kenmore, declared that his Alma Mater and the Commonwealth of Massachusetts are two pioneer agencies in the original study and continuing development of this field.

"Psychiatry," he said, "like other branches of medicine has much to learn but it presents a fertile field for research."

The dinner was featured by a special reunion of the 10-year class of 1926 under the direction of Dr. Ralph Wells of Newton Centre. Dr. Cecil Clark of Newton, toastmaster, introduced the speakers who, in addition to Dr. Overholser, included: Dr. Daniel L. Marsh, President of Boston University; Dr. Alexander S. Begg, Dean of the School of Medicine; Dr. Reginald Fitz, Director of the Evans Memorial; Dr. Howard Clute, Professor of Surgery; and Walter Mulvihill of Worcester, president of the senior class. Dr. Rudolph Jacoby of Newton, and Dr. Samuel N. Vose of Newton Centre, arranged the dinner.

Officers for 1936-37, who were elected, are the following doctors: President, David L. Belding '13, Hingham; First Vice-President, C. Wesley Sewall '14, West Roxbury; Second Vice-President, Nathan H. Garrick '15, Boston; Secretary, Rudolph Jacoby '11, Newton; Treasurer, Harold W. Ripley '17, Braintree; Auditor, Samuel N. Vose '18, Newton; Directors, Frank E. Barton '24, Newton; Cecil W. Clark '15, Newton; Leighton F. Johnson '15, Norwood; John A. Rockwell '99, Cambridge; Helmuth Ulrich '11, Newton.

Speaking further on the importance of psychiatry, Dr. Overholser said: "The field of psychiatry has long since outgrown the walls of what were formerly known by the dismal name of 'asylums.' Today, psychiatry is no longer the orphan of medicine, but is recognized generally as a specialty which has its bearing on every other specialty of medicine. The surgeon, the internist, everyone who today is dealing with the sick, is recognizing more and more the importance of mental factors in disease and the fact that physical disorders have their mental concomitants. This fact was recognized in different terms by the men who founded the Boston University School of Medicine, and it is gratifying to us, as alumni of that school, to realize that the founders were men who were ahead of their times.

"Psychiatry, in addition to its contacts with other branches of medicine, comes into touch with many community activities as well. I need hardly mention to you the program in which Massachusetts was a leader, dealing with the early recognition of mentally retarded children in the public schools; of that pioneer activity of Dr. Thom in developing the habit clinics in the child guidance work; and of the important pioneer activity of Massachusetts under the Briggs law of assisting the courts in their difficult task of dealing with defendants on the basis of a knowledge of their mental condition. It is pleasing to note that this latter activity has been recognized by the Federal Department of Justice and Public Health Service in selecting Boston as the first place in the country to establish in the Federal Courts a system of psychiatric advisers to the Court.

"Psychiatry, like other branches of medicine, has much to learn, and presents a fertile field for research. Much research is being done, both in Massachusetts and elsewhere, under the auspices of the State and of private foundations. Much needs to be learned about the method of prevention of mental disorders and, in this field again, psychiatry has a heavy obligation to the community in which it must not be found wanting.

"The Commonwealth of Massachusetts, through its Department of Mental Diseases, is giving every possible encouragement to the work of research and prevention. Massachusetts was indeed the first state to recognize by statute the fact that a state, even if it gives every possible care to the mental patients within its hospitals, is not fulfilling its entire duty to the community unless it takes steps to direct research activities toward the prevention and earlier cure of mental disorders with a view, not only to decreasing the sum total of human misery, but of lessening, as well, the burden upon the taxpayers of supporting its ever-growing institutions."

THE INTERNATIONAL CONGRESS OF PHYSICAL MEDICINE AND PHYSIOTHERAPY

The sixth International Congress of Physical Medicine and Physiotherapy which was held in London, May 12 to 16, 1936, under the patronage of the British Government, was attended by widespread attention throughout England. The section on Physical Education was a prominent feature of the program which contained reports on recent developments in all branches of physical medicine and physical therapy. It was presided over by Sir Robert Stanton Woods, M.D., one of the physicians to the late King George.

At this Congress Dr. William D. McFee was elected to Honorary Membership in the permanent organization, the International Association of Physical Medicine and Physiotherapy, this being the first time this honor has been conferred by the association.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

The April meeting of the New England Ophthalmological Society was held April 21 in the Massachusetts Eye and Ear Infirmary. After the reading of the minutes of the previous meeting, Dr. Benjamin Sachs presented the first case: A forty year old Italian male entered complaining of pain in the eyes of four weeks' duration, photophobia, ptosis, but no loss of vision. A bilateral enlargement of the lacrimal glands was found, each being about the size of an almond, the eyes being red and dry and there was evidence of old posterior synechia on the left. The Hinton was negative and the patient was given potassium iodide. A chest plate showed marked hilus thickening and it was felt that the condition was probably due to tuberculosis. A diagnosis of dacryo-adenitis was made.

Dr. Sachs next presented a fifty-six year old male who has been treated for syphilis since 1902, had gonorrhea in 1904 and pulmonary tuberculosis in 1917. Examination showed a yellow jelly-like mass under the conjunctiva on the left eye without accompanying symptoms. There were other small, nodular swellings involving both lids of both eyes as well as in the neck and legs. The patient showed an eosinophilia of 6 per cent. It was felt that this was probably a case of sarcoma of kaposi, which condition is said to respond well to arsenic and x-ray treatment.

Dr. Sachs then presented a case of stellate retinitis, that in May, 1935, presented a small right paracentral scotoma. This winter the patient developed grippe and following this noticed black spots before his right eye. In January a swelling of the right disc and a vitreous opacity was noted. Under observation this patient developed pathology involving the macula and a typical star-shaped figure was demonstrated. The blood pressure, skull plates and urine were negative.

Dr. Sachs then presented a case of unilateral exophthalmos which has developed following subtotal thyroidectomy in July 1935. The question arose as to how to stop this process, but without a definite decision.

The next patient had been struck on the head, five years previously. He was unconscious for two hours and some months later noticed a hard lump on the forehead. The patient had had dizzy spells which terminated in profuse epistaxis and foul discharge from the nose, and he had also had several epileptiform attacks. Gradually he developed exophthalmos and a severe pain in both eyes during the past few weeks. Examination showed a nontender, hard mass, not fixed to the skin in the midforehead, exophthalmos, rather swollen lids and a limitation of the movements of the eyes. The fields and fundi were normal. Neurological examination and spinal fluid were normal. Skull plate showed destruction of the frontal bone and ethmoid. A diagnosis has not yet been made.

Dr. James Regan presented a case of a girl who, following spinal anesthesia, developed photophobia and limitation of motion of the right eye due to paralysis of the right abducens nerve. During the three months since that time she had gradually improved. There are several examples in the literature of ophthalmoplegia following the administration of spinal anesthesia. Of these, paralysis of the sixth nerve is most common, but such cases usually clear up much more quickly than in this instance.

The seventh case was monocular pigmentary degeneration of the retina. There are eight other authentic cases reported in the literature. Dr. Wells demonstrated a pair of spectacles that can be used, while the patient is lying on his back, for reading at right angles.

Dr. Algernon B. Reese delivered the paper of the evening on "Changes that Occur in a Detached Retina." The frequency with which central vision is poor following operations for re-attachment of the retina is well known. Statistics show that about 32 per cent of such patients give a central vision of 20/30 or better after re-attachment. It was also shown that the lapse of time between attachment of the retina and operation was an important factor. Microscopic examination of the detached retina shows that there are cystic spaces formed, especially in the region of the macula. Those cases that

come to microscopic examination are usually far advanced, but occasionally a sarcoma is suspected and an enucleation performed when the detachment is recent. Some of these cases have been carefully studied by Dr. Reese and he showed numerous lantern slides to demonstrate the cysts which occur even in the youngest cases. Occasionally these cysts can be seen clinically, but usually not. Near the cysts a gliosis occurs which replaces the rods and cones. Cases with duration of four years down to about two weeks were shown. Besides the cysts which occur in Henle's fiber layer, there is also a wrinkling of the internal limiting membrane of the retina. Although the cysts can only rarely be seen by ophthalmological examination, the wrinkling of the internal limiting membrane can be seen frequently. By using a beam of light cast to the side of the lesion, if the macula is close to the choroid, these cysts may frequently be seen by reflected light, similar to objects seen in a dark-field examination. The radiating rarefied lines can never be seen by direct examination. The Scotch grain leather appearance is probably due to the wrinkling of the internal membrane. After attachment the cysts disappear and pigment is later laid down. Cysts may be of various other etiologies such as (1) post-traumatic (2) complication of iridocyclitis (3) retinitis pigmentosa (4) in central vein thrombosis (5) spontaneous cysts. It is felt that the cysts occurring in detachment of the retina and which occur in the external plexiform layer of Henle's are due to edema from the altered circulation of the retina. These occur especially at the macula because it is at this point that the circulation is least satisfactory. Following attachment of the retina there is a slow improvement of central vision over many months due to the disappearance of the edema. If the edema has been of sufficient duration, however, there is an atrophy of the neural elements, and vision will be impaired permanently. Holes in the retina are extremely rare and most of the conditions that appear to be holes are really cysts.

The white lines seen so commonly in detachment of the retina are due to the limitation of the detachment during a certain period which leads to a glial proliferation along the edge and this is seen as a white line clinically.

In conclusion, Dr. Reese said that even though two-thirds of the cases of detached retinae which were operated on will have poor vision, certainly it is important to operate on them because many of them within a few years are apt to develop a uveitis leading to a secondary glaucoma necessitating enucleation.

NEW ENGLAND PHYSICAL THERAPY SOCIETY

Notice of Adjourned Annual Meeting

The Annual Meeting of the New England Physical Therapy Society was by vote of the meeting of May 20, 1936, adjourned to June 8, 1936, to be held at the Hotel Kimball, Springfield, Massachusetts, immediately following the program of the Section of Radiology and Physiotherapy of the Massachusetts Medical Society. The usual business of the Annual Meeting will be transacted at that time.

Members are asked to refer to the program for the Annual Meeting of the Massachusetts Medical Society for details concerning the excellent papers to be presented at Springfield. All members of this Society are urged to be present.

William D. McFee, M.D., *Secretary.*

Boston, Mass.

SOUTH END MEDICAL CLUB

The next regular meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, Tuesday, June 16, 1936, at 12 noon. The speaker will be Louis E. Phaneuf, M.D., Professor of Gynecology, Tufts College Medical School; Gynecologist and Obstetrician-in-Chief, Carney Hospital. His subject will be "Pelvic Infection in Women." Lantern slides will be shown. All physicians are cordially invited to attend. Luncheon will be served at 1 o'clock.

NEW ENGLAND ALUMNI—DINNER MEETING

University of Maryland School of Medicine
College of Physicians and Surgeons
Baltimore Medical College, Baltimore

Annual dinner at Hotel Highland, Springfield, Tuesday, June 9 at 12:30.

Dr. M. W. Harrington (B. M. C. 1901).
Dr. M. F. Hosmer (P. & S. 1914).
Dr. A. H. Riordan (U. of M. 1915).
Springfield Committee.

SOCIETY MEETINGS, CONGRESSES AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING MONDAY, JUNE 8, 1936

Wednesday, June 10—

†12 M. Clinico-Pathological Conference. Children's Hospital.

Thursday, June 11—

*8:30-9:30 A.M. Clinic, Surgical Staff of the Peter Bent Brigham Hospital, at the Peter Bent Brigham Hospital.

Saturday, June 12—

*10 A.M. - 12 M. Staff Rounds at the Peter Bent Brigham Hospital. Conducted by Dr. Henry A. Christian.

*Open to the medical profession.
†Open to Fellows of the Massachusetts Medical Society.

June 4, 5, and 6—Annual Meeting of the American Dermatological Association at the New Ocean House, Swampscott.

June 4 - July 3—Massachusetts Institute of Technology Department of Biology and Public Health. See page 1012, issue of May 14.

June 8—Tufts Medical Alumni Luncheon. See page 1047, issue of May 21.

June 8—New England Physical Therapy Society. See notice elsewhere on this page.

June 8, 9, and 10—American Association for the Study of Goiter. See page 1075, issue of May 21.

June 9—New England Alumni. See page 1170.

June 9—Massachusetts Medico-Legal Society. See page 1047, issue of May 21.

June 9—Massachusetts Diplomates of the National Board of Medical Examiners. See page 1047, issue of May 21.

June 15-19—The Executive Board of the Catholic Hospital Association will meet at the Fifth Regiment Armory, Baltimore, Md.

June 16—South End Medical Club. See page 1170.

June 16 - July 28—Summer Course in Bacteriology. See page 385, issue of February 20.

June 21-23—Maine Medical Association at Rangeley, Maine.

June 22 and 23—The Medical Library Association. See page 1075, issue of May 21.

June 29 - July 11—Hospital Administration. See page 957, issue of May 7.

August 24-29—Harvard University Tercentenary Celebration. See page 1166.

September, 1936—First International Congress of Sanatoria and Private Nursing Homes. See page 803, issue of April 16.

September 7-10—International Union against Tuberculosis. See page 554, issue of March 12.

September 14 and 15—Tercentenary Session of the Harvard Medical School. See page 1166.

September 29 - October 3—First International Conference on Fever Therapy. See page 1325, issue of December 26, 1935, and page 1075, issue of May 21.

October 12-18—Third International Congress on Malaria. See page 1076, issue of May 21.

October 19-23—Clinical Congress of the American College of Surgeons. See page 180, issue of January 23.

April 21-24, 1937—American Society for Experimental Pathology. See page 1075, issue of May 21.

BOOKS RECEIVED FOR REVIEW

Examination of the Patient and Symptomatic Diagnosis. John Watts Murray. Second Edition. 1219 pp. St. Louis: The C. V. Mosby Company. $10.00.

International Clinics. Volume I. Forty-Sixth Series, 1936. Edited by Louis Hamman. 314 pp. Philadelphia, Montreal, London: J. B. Lippincott Company.

Medical Mycology. Fungous Diseases of Men and Other Mammals. Carroll William Dodge. 900 pp. St. Louis: The C. V. Mosby Company. $10.00.

The Specificity of Serological Reactions. Karl Landsteiner. 178 pp. Springfield and Baltimore: Charles C Thomas. $4.00.

The Single, The Engaged, and The Married. Maurice Chideckel. 268 pp. New York: Eugenics Publishing Company. $2.50.

An Index of Differential Diagnosis of Main Symptoms of Various Writers. Edited by Herbert French. Fifth Edition. 1145 pp. Baltimore: William Wood & Company. $16.00.

Medical Papers. Dedicated to Henry Asbury Christian, Physician and Teacher. Editor, Robert T. Monroe. 1000 pp. Baltimore: Waverly Press, Inc.

A Synopsis of Physiology. A. Rendle Short and C. I. Ham. Second Edition. Edited by C. L. G. Pratt. 312 pp. Baltimore: William Wood & Company. $3.50.

Lectures on Diseases of Children. Robert Hutchison. Seventh Edition. 452 pp. Baltimore: William Wood & Company. $6.75.

An Introduction to Surgery. Rutherford Morison, and Charles F. M. Saint. Third Edition. 367 pp. Baltimore: William Wood & Company. $5.00.

A Textbook of Surgery by American Authors. Edited by Frederick Christopher. 1608 pp. Philadelphia and London: W. B. Saunders Company. $10.00.

Your Hay Fever. Oren C. Durham. 264 pp. Indianapolis and New York: The Bobbs-Merrill Company. $2.00.

Convalescent Care in Great Britain. Elizabeth Greene Gardiner. 163 pp. Chicago: The University of Chicago Press. $1.50.

BOOK REVIEWS

The Medicine-Man of the American Indian and His Cultural Background. William Thomas Corlett. 369 pp. Springfield and Baltimore: Charles C Thomas. $5.00.

The history of the American Indian has always borne a fascination for the American physician, and Dr. Corlett's book, a profound study of his "Medicine Man" and his cultural background, will prove a delight to many.

The work is divided into five parts taking up such subjects as "Racial Origin", "Medicine Men of the New World", dealing with the Shaman as he appears in different sections of North and South America, "Childbearing", "Food and Materia Medica of the Indian", and, finally, the "Closing Day."

One of the most interesting parts is that on "Racial Origin" and the Indians' migration across Behring Sea from Siberia. Most of us do not realize the extremely short distance separating Siberia and Alaska which an aeroplane can traverse in less than one-half hour.

It is interesting also to note that the Mayas had a symbol for zero over one thousand years before it was invented by the Hindus.

Corlett tells us that Nezahualcoyotl, who died in 1472, was a chief of the Chichimecas, a tribe dwelling near the Aztecs. He said: "The things of yesterday are no more today; and the things of today shall cease, perhaps on the morrow. These burying grounds are full of the loathsome dust of bodies, once quickened by living souls, who occupied thrones, presided over assemblies, marshalled armies, subdued provinces, arrogated to themselves worship, were puffed up with vainglorious pomp, and power, and empire. But all of these glories have passed away, like the fearful smoke that issues from the throat of Popocatepetl, and with no other memorial of their existence than the record on the page of the chronicler.

"The great, the wise, the valiant, the beautiful—alas! where are they now? They are all mingled with the clod; and that which has befallen them shall happen to us, and to those that come after us. Yet let us take courage, illustrious nobles and chieftains, true friends and loyal subjects, let us aspire to that heaven where all is eternal and corruption cannot come. The horrors of the tomb are but the cradle of the Sun, and the dark shadows of death are made brilliant by the light of the stars."

Corlett further states that this chief of the Chi-

chimecas left behind him "a record of the highest civilization North America had known."

The author informs us in his summary of the Medicine-Men that the theory of disease-cause which is most universal and popular in the New World, is that of the disease-object intrusion. This is the theory which holds that sickness is due to the presence in the body of some foreign object, such as a fish-bone, a stick, a stone, or a bit of hair. In addition, the following causes for illness, given in descending order of their importance, may be listed: soul-loss, sorcery, spirit-intrusion, and finally, breach of taboo.

He further tells us that the supernatural of course plays a major part in all the Indian's healing ceremonies. But the medicine-man's job is to inspire faith on the part of his patient, and to use some common sense in his treatment. Even today, he says, the treatment of many a modern charlatan is often as harmful and horrible as that of the Indian medicine-man.

There is much of great interest in the part of the book devoted to child-bearing in the Indian races.

Surely the lover of Indian history will be impatient to read the fascinating pages of Dr. Corlett's book.

Aids to Medicine. James L. Livingstone. Fifth Edition. 422 pp. Baltimore: William Wood and Company. $1.50.

This is a compendium of medical knowledge which is one of a series of "Students' Aids" printed in Great Britain and distributed here by William Wood and Company. It is a volume of four hundred odd pages, four by six and a half inches and three-quarters of an inch in thickness, making a handy pocket volume for medical students to read in the subways and other such places. It covers a comprehensive variety of diseases and for that reason makes interesting random reading. The views expressed are essentially conservative and sound.

Venereal Disease Information. Prepared by the U. S. Public Health Service. Washington: Government Printing Office.

It is the purpose of the Public Health Service in issuing this publication to provide in condensed form a monthly summary of the scientific developments in the diagnosis, treatment, and control of syphilis and gonorrhea. More than three hundred American and foreign journals are reviewed for this work. Abstracts are made of articles describing laboratory, pathologic, and clinical work in the field of venereal diseases.

The most important literature on every phase of the subject is presented in the form of brief abstracts that are easily read. An index for the year is published with the December issue.

During the past year thousands of physicians found this publication useful in enabling them to keep abreast with developments in venereal disease work.

The cost of this publication is only fifty cents per annum, payable in advance to the Superintendent of Documents, Government Printing Office, Washington, D.C. It is desired to remind the reader that this nominal charge represents only a very small portion of the total expense of preparation, the journal being a contribution of the Public Health Service in its program with State and local health departments directed against the venereal diseases. If you wish to secure the valuable service which this monthly magazine provides, send fifty cents to the Superintendent of Documents, Government Printing Office, Washington, D.C.

Demonstrations of Physical Signs in Clinical Surgery. Hamilton Bailey. 287 pp. Fifth Edition, Revised. Baltimore: William Wood and Company. $6.50.

The popularity of this volume is evidenced by the fact that five editions have been required since it first appeared in 1927. Practically every physical sign of value in surgical diagnosis is clearly yet briefly described. The very generous use of illustrations, many of them colored, adds greatly to its clarity. It has proved itself a most useful book for both students and practicing physicians.

Les Acquisitions Nouvelles de L'Endocrinologie. R. Rivoire. 305 pp. Paris: Masson et Cie. 36 fr.

This book on newer conceptions in endocrinology is well written and exceptionally well up-to-date. The reviewer has checked certain data contained in this monograph, and he found them remarkably accurate.

There are six chapters in all. One each is devoted to parathyroid, suprarenal, pancreas, ovary, testes, and pituitary glands.

It makes easy and interesting reading to one conversant with French and the price is reasonable. It is a valuable addition for the endocrinologist.

Diseases of the Nose and Throat for Practitioners and Students. C. J. Imperatori and H. J. Burman. 723 pp. Philadelphia: J. B. Lippincott Company.

This volume is designed as a textbook for the general practitioner and the senior medical student. It gives a description of many of the more common diseases and a few of the less common ones, and discusses their symptoms, diagnosis, treatment, pathology and causation. It is in outline form and is carefully illustrated.

Considering the point of view of the readers for whom the book is intended, there is far too much emphasis on the details of operative technique. Many of the more serious illnesses, moreover, such as malignant neoplasm, have been treated in a very superficial manner. The book is well prepared from a publisher's standpoint, but as a textbook it is superfluous, since there are many other excellent treatises on the same subject.